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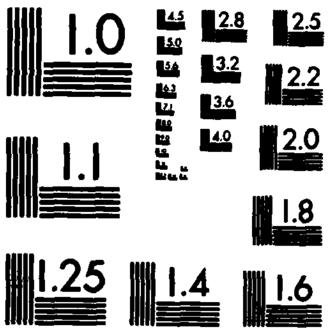
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European Science Notes

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July 1985
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Behavioral Sciences

In psychology, much effort has been invested in developing statistical models by which reliability of measurements can be estimated under specified conditions. Now several European researchers have advanced the development of "generalizability theory," the integration of partial models into a general approach. in the Behavioral Sciences

Biological Sciences

The Institute for Biotechnology of the Swiss Federal Institute of Technology is doing first-class work that is making important connections between basic and applied areas of biotechnology. This article discusses research on yeasts, microbial surfactants, biological degradation of lignin, thermophilic organisms, and control of bioprocesses.

ETH-Zurich's Institute for Molecular Biology and Biophysics and Institute for Molecular Biology I do first-rate work with relatively small staffs. This article looks in detail at work in areas such as neuropeptides and hormones, protein structure and enzymology, gene function, interferon, and molecular virology.

Researchers at ETH-Zurich's Institute for Molecular Biology II are examining the interplay of the genetic factors in organisms such as mice, frogs, and sea urchins. This article examines work on activation of the immunoglobulin gene in B-lymphocytes, the regulation of the expression of the histone gene, and the RNA scripts of genes.

Researchers in the Department of Cell Biology of ETH-Zurich believe that the technique of freeze-etching can provide a better understanding of the fundamental building blocks that make up biological structures.

Con't

Mechanics

Quantitative experimentation coupled with linear stability calculation and computer graphic displays of streakline and vorticity evolution is providing new answers to organized behavior--such as vortex pairing--in turbulent shear flows.

Physics

Some unusual features of Spain's research infrastructure in areas such as modern optics, microelectronics, lasers, nonlinear dynamics, and expert systems are informally reviewed. Possibilities for productive cooperation are pointed out.

Closely related areas of research in modern optics, solid state physics, thin films, and microelectronics at three universities and two government research institutes in Madrid are surveyed and assessed. Topics covered include optical bistability, fiber research, gas lasers, nonlinear optical materials and phenomena, crystal growing, laser instabilities, thin film preparation/modification, electron beam stimulated oxidation, and molecular beam epitaxy.

Science Policy

The Centre National de la Recherche Scientifique (CNRS) is the largest organization and the most influential authority in directing and financing basic and applied scientific research in France. This article provides an overview of CNRS's organization and mission.

The Council of Ministers of the European Economic Community has approved a telecommunications R&D program called RACE, for R&D in Advanced Communication Technology for Europe. This article discusses the program's background, rationale, and objectives.

News and Notes

* * *

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Behavioral Sciences

RECENT EUROPEAN CONTRIBUTIONS TO MEASUREMENT THEORY

by Richard E. Snow. Dr. Snow is the Liaison Scientist for Psychology in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on leave until September 1985 from Stanford University, where he is Professor of Education and Psychology.

Reliability of measurement is fundamental to all science; a measure is useful only as it informs us of the expected value of other measures taken under equivalent conditions. But conditions are never exactly equivalent; they are samples from a multifaceted space of possible conditions, and sampling variation across some of these facets can sometimes be substantial. Thus, in psychology much effort has been invested in developing statistical models by which reliability of measurements can be estimated under specified conditions. Various partial models, developed earlier, have been integrated into a general approach, called "generalizability theory," by Cronbach, Gleser, and Rajaratnam (Cronbach, Rajaratnam, and Gleser, 1963; Gleser, Cronbach, and Rajaratnam, 1965; Cronbach, Gleser, Nanda, and Rajaratnam, 1972; for reviews of further US developments, see Brennan, 1983, and Shavelson and Webb, 1981). Recent work by Swiss, Belgian, German, and Norwegian researchers has also advanced the development of generalizability theory in several ways.

The theory of Cronbach et al. established the sampling view of psychometrics sketched above and specified the methods by which one should investigate the conditions of measurement in question and estimate the degree to which one might generalize to other conditions. No single estimate reflects a measure's reliability; rather, there are different estimates that apply to generalizations across different facets of the measurement conditions.

However, some apparent limitations on generalizability theory have been recognized. First, the theory is asymmetrical in accepting, at least implicitly, the traditional psychometric view that the aim of measurement is always differentiation among persons, or groups of persons; today in psychological and educational research, the aim is often differentiation among items or tasks, alternative educational or therapeutic treatments, or moments in time, for example. Second, generalizability theory as developed and typically applied is multivariate with respect to the conditions of measurement but univariate with respect to the objects of measurement. Although Cronbach et al. formulated an approach to estimating the generalizability of aptitude profiles, for example, there has not been much further exploration of cases of multivariate dependent measures, or comparisons with other multivariate approaches. Now, a collaboration among French-speaking Swiss and Belgian researchers has addressed the first problem. One German and one Norwegian psychometrician have attacked parts of the second problem, while another German has pursued a third problem relevant to both previous problems--namely, the need to understand and control the cognitive psychology of test item differences. (Characteristically, the French- and German-speaking researchers did not seem to know of one another's work--they do now, thanks to ONR, London.)

The Problem of Symmetry

Because the initial development of generalizability theory focused on psychometric uses, the facets of concern in evaluation *designs* were those that varied over measurement conditions, e.g., moments in time, observers, test forms, rating scales, etc.; these were the conditions over which generalization would be needed in future uses of the measure. Persons were not considered a facet, but rather the dimension along which differentiation was to be studied. But Cardinet, Tourneur, and Allal (1976, 1981) have argued correctly that generalizability theory applies to a much wider range of measurement problems if it is made symmetrical. Persons, and the various ways in which persons might be divided, should also be considered facets. And the theory applies to the differentiation of *any* objects of study, whether persons, methods of treatment, school systems, training programs, types of items, stages of learning, etc. Thus, the symmetrical possibilities of study design should always be considered. What facets are defined for a particular design, and what facets are to be considered as fixed or random, depend on the purposes of measurement and the goals of generalization.

Cardinet, Tourneur, and Allal define the "face of generalization" as those facets reflecting sources of variation to be considered error in a

particular study, i.e., those over which generalization is desired. The "face of differentiation" is then defined as those facets within and between which a given study seeks comparisons. The Cartesian product of all the facets of generalization identifies the set of all possible conditions of observation in the study. The Cartesian product of all the facets of differentiation identifies the set of all possible comparisons among the objects of study.

A further important point is that both the faces of generalization and of differentiation can include facets of three possible types: *fixed* facets, in which the levels of the facet are chosen to exhaust the universe of admissible levels; *random* facets, in which the levels are considered a random sample of levels from a hypothetically infinite universe of levels; and facets that are *random* samples from a *finite* universe of admissible levels. The random versus fixed versus random-finite designation must be made independently for each facet and has important implications for the estimation model ultimately designed. Cardinet, Tourneur, and Allal (1981) and Cardinet and Allal (1983) have given detailed analyses and examples of several designs embodying their principle of symmetry with both fixed and random facets. The possibility of random-finite facets has not yet been developed because no general statistical solution yet exists for unbiased estimation of variance components for such facets. The explication of all this is an important contribution because symmetry, and the possibilities of fixed and finite sample facets, have not been fully examined to date in generalizability theory.

Cardinet and Allal (1983) provide a four-phase framework for the decisions and calculations that need to be made in conducting generalizability analyses (Figure 1). Phase 1 is the observation design that specifies the set of observed data and identifies the facets. Phase 2 considers the estimation design, specifying the character of sampling for each facet. Phase 3 is the measurement design that distinguishes the differentiation facets and generalization facets (generalization facets are called "instrumentation" facets by Cardinet and Allal [1983], and this term thus appears in Figure 1). Phase 4 is the optimization design that identifies the modifications needed to provide sufficiently precise estimation for the desired measurement. The authors also provide substantial computational examples. Readers concerned with the measurement of educational comparisons involving objects other than persons should find the development by Cardinet, Tourneur, and Allal especially helpful.

The Problem of Multivariate Measures

The German work on multivariate reliability comes from Wittman (1982; in press). Wittman sees his approach as stemming from the Brunswikian tradition in German-Austrian psychology and aiming at a resolution of some of the complexities of person × situation interaction phenomena (see *ESN* 39-3:71-78 [1985]). Generalizability is a matter of transsituational, transpersonal, and transinteractional consistency. Methods of covariance partitioning are thus needed to examine the response of measures to situation, person, and interaction variance in particular samples in which measures are expected to serve particular purposes. The concepts of reliability and construct validity need careful delineation in this context, especially with respect to substantive rather than purely psychometric theory.

To attack this problem, Wittman characterizes the universe of measurement concern in terms of Cattell's basic data-relations matrix and employs a combination of multivariate analysis of variance and factor analysis to explore this matrix. The choices typically called for in generalizability theory are made within this context. Usually for explication, however, the 10 coordinates of this matrix are collapsed to the more widely known, three-dimensional Cattell covariation chart. This of course focuses the reliability analysis on person × occasion consistency. Measurement theory formulas are recast in this multivariate framework. Factor analysis is used both to explore the universe of concern and to confirm particular causal models proposed for it.

The formulation is difficult to follow, but several computational examples are given to apply the approach to existing data on state anxiety questionnaires. According to Wittman, the methods of covariance partitioning proposed make it possible to examine the response of test instruments to person, situation, and interaction variance and to bring state and trait measures together in a common multivariate analysis. Several projections of these ideas for future research are discussed.

Some particularly important special cases of multivariate reliability have been attacked by Eikeland (1972, 1973) in Norway. One concerns the fact that many educational and psychological measures used in practice are hierarchically stratified. In these instruments, items may be regarded as randomly sampled but

Model	Phase	Information regarding the facets	Type of design	Result of calculations	Symbols	Steps in carrying out the calculations
ANALYSIS OF VARIANCE	1	Identification - choice of facets - relationships among facets (crossed, nested, confounded) - number of observed levels (per facet) *Specifies the set of observed data*	Ob-ser-va-tion	Mean squares	α	1 Source of variation : Identify the sources corresponding to all main effect and interaction effects. The total subscript of an effect (α) is noted as follows: (primary subscript(s)) : (1st nesting subscript(s)) : ... : (nth nesting subscript(s)), e.g. (ip:c:s) for the interaction of items with pupils nested in classes nested in schools.
					$MS(\alpha)$	2 Mean squares : Compute the mean square for each effect (α). (See Millman and Glass, 1967).
	2	Sampling Number of admissible levels and mode of sampling determine whether a facet is : . purely random . finite random . fixed *Specifies the domain of admissible observations*	Es-ti-ma-tion	Variance components, random or mixed model	$\hat{\sigma}^2(\alpha)$	3 Random model variance components : For each effect (α) comput[e] $MS(\alpha) + \sum_{i=1}^{i=j} (-1)^i$ {sum of the mean squares whose total subscripts contain α plus the letter(s) for i additional facet(s), each of which appeared in subscripts at step (i - 1) for i > 1 where (i) is the rank (from 1 to j) of the expression betw[een] parentheses {} and (j) is the number of such expressions. Divide this expression by $f(\alpha)$, the product of the numbers of observed levels of all facets not appearing in the total subscript of the effect (α).
					$\hat{\sigma}^2(\alpha\|M)$	4 Mixed model variance components : For a design with one or more fixed and/or finite facets, the mixed model estimate is: $\hat{\sigma}^2(\alpha\|M) = \hat{\sigma}^2(\alpha) + \sum_j \frac{\hat{\sigma}^2(\beta_j)}{f(\beta_j)}$, where $\hat{\sigma}^2(\beta_j)$ = random model estimates of all other components, which include all letters of the component (α) in their total subscript $f(\beta_j)$ = product of the numbers of admissible levels of the facets appearing in the subscript of β_j but not in the subscript (α) Carry out subsequent calculations using the components obtained in this step
THEORY OF GENERALIZABILITY	3	Role in measurement - Differentiation face: D facets . random D facets: D^R . fixed D facets: D^F - Instrumentation face: I facets . random I facets: I^R . fixed I facets: I^F *Specifies the population of admissible objects of measurement and the universe of admissible conditions of measurement*	Mea-su-re-ment	Allocation of the facets of the measurement design and specification of the active variance components	$M(D^R/D^F/I^F/I^R)$	5 Measurement design(s) : Define one or more design(s) to be analysed by steps 6 through 12. 6 Control of coherence : Verify that there are no D facets nested within I facets, confoundind D-variance and error. 7 Active variance : Eliminate components having I^F facet(s) in their primary subscript. 8 Expectancies of variance : Multiply components by $(N_f - 1)/N_f$ for each fixed or finite facet in their primary subscript.
				Differentiation variance	$\delta^2(\tau)$	9 Differentiation variance : Extract from the active variance and sum all components which includ[e] only D facets in their primary subscript.
				Error (generalization) variances	$\delta^2(\Delta)$	10 Absolute error variance : Sum all the remaining components, each weighted by $(1/n_i)$ for each I facet in its total subsc. & by $(N_i - n_i)/(N_i - 1)$ for each finite I facet in its primary subsc.
					$\delta^2(\delta)$	11 Relative error variance : Extract from the preceding expression and sum with their coefficients all components which include at least one D facet in their total subscript.
				Generalizability coefficient	$\hat{E}\rho^2$	12 Generalizability coefficient(s) : Divide the differentiation variance by the sum of the differentiation variance and the error variance under consideration ($\delta^2(\delta)$, $\delta^2(\Delta)$).
	4	Modifications - Relationship among facets (nesting or confounding of previously crossed facets) - Number of observed levels (increased for I^R facets) - Number and mode of sampling of admissible levels of D or I facets *Specifies the recommended population(s) of differentiation and universe(s) of generalization*	Op-ti-mi-za-tion	Allocation of facets of optimization design and specification of active variance components	$O(D^R/D^F/I^F/I^R)$	13 Optimization design(s) : Define one or more design(s) taking into consideration modifications of the initial observation, estimation and measurement designs, in order to decrease error, to improve validity, or to decrease costs. Repeat, as appropriate, steps 3 to 8.
				Differentiation variance	$\delta^2(\tau')$	14 Differentiation variance : Repeat step 9.
				Error (generalization) variances	$\delta^2(\Delta')$ $\delta^2(\delta')$	15 Error variances : Repeat steps 10 and 11.
				Generalizability coefficient	$\hat{E}\rho^2$	16 Generalizability coefficient(s) : Repeat step 12.

Figure 1. Framework for conducting generalizability analyses (from Cardinet and Allal, 1983).

nested within strata, and there may be lower order strata nested within higher order strata. The strata at any level may be regarded as fixed or random. Multilevel aptitude and achievement batteries are often of this type. Yet no satisfactory mathematical models have been developed for such tests. Eikeland (1972) has thus developed a family of models based on the application of

generalizability theory to the variance-covariance matrices typical of these sorts of tests. He shows with numerical examples how generalizability estimates can be derived for scores at the several levels of such tests, under various combinations of fixed and random facet assumptions. He also argues that the development offers a general structural theory for other kinds of complex test designs, and traces the framework back to the rationale of the original Spearman-Brown formulation.

The other special case arises from the use of difference scores to characterize psychological constructs or the differential validity of predictors for performance in alternative treatments. Eikeland (1973) notes that different uses of difference scores may be subject to somewhat different kinds of limitations in practice, but that, given a sound logic for the differential construct, the analysis of reliability of any such construct should proceed within the framework of generalizability theory. As in any generalizability problem, the correct model depends on the specific test design underlying the difference scores to be used. Eikeland shows that for the complex test designs of today the traditional formulation of the reliability of a difference is completely out of date. Again, since a family of possible difference scores is of potential interest, a family of models needs to be considered. He thus derives new formulations, based on the Spearman Brown prophecy formula, for a variety of combinations of sum and difference scores, and for several combinations of fixed and random test design facets.

The Cognitive Psychology Problem

The implications of new developments in cognitive psychology for educational and psychological measurement are many. Some of these also couple with advances in the technology of computerized adaptive testing. A central concern in all this is the design of cognitive tests as within-person experiments. Such designs use experimental facets in both the face of generalization and the face of differentiation; these facets may be considered fixed or random or random-finite. They provide new kinds of multivariate dependent variables, since the computer allows error, latency and even confidence scores from each item performance; these scores are experimentally dependent. Such designs are also often hierarchically stratified. The scores of theoretical interest are often complex contrast, or difference, scores.

Thus, this convergence of problems and potentials needs to be carefully considered in the context of generalizability theory, and all of the new developments mentioned above apply. To this reporter's knowledge, no one has yet taken on this awesome task. But bits and pieces of what is needed are beginning to appear.

One piece comes from the work of Hornke (1977, 1981; see also Mispelkamp, n.d.) and his collaborators in Germany. They are developing item construction theories for cognitive measures, such as the Raven Progressive Matrices Test, and also affective measures, such as the Mannheim Anxiety Scale. Work has also begun on tests for diagnosing text comprehension. The goal is to formulate taxonomies of item characteristics that systematically represent the logical and psychological structure of performance. They specify, in other words, the content and construct validity of tests in a new way. This should allow controlled item construction or selection in computerized adaptive, or response-contingent testing.

So far, results suggest some problems for conventional item-response models. Such models reject items that do not fit certain mathematical functions. But the items (and person responses) thus rejected turn out to be systematically different psychologically from selected items. Uncritical use of purely psychometric models in conventional, and especially in computerized adaptive, testing can distort the substantive content and construct meaning of the measure appreciably. This is an important problem for selection testing; it is absolutely critical for diagnostic testing.

All this argues for new coordinated research on the generalizability theory of psychological assessment. Both the psychological and the psychometric theory of assessment need concentrated attention.

References

Brennan, R.L., *Elements of Generalizability Theory* (Iowa City, Iowa: ACT Publications, 1983).

Cardinet, J., and L. Allal, "Estimation of Generalizability Parameters," in *Generalizability Theory: Inferences and Practical Applications*, ed. L.J. Fyans, Jr. (San Francisco: Jossey-Bass, June 1983).

Cardinet, J., Y. Tourneur, and L. Allal, "The Symmetry of Generalizability Theory: Applications to Educational Measurement," *Journal of Educational Measurement*, 13 (1976), 119-135.

_____, "Extension of Generalizability Theory and its Applications in Educational Measurement," *Journal of Educational Measurement*, 18 (1981), 183-204.

Cronbach, L.J., G.C. Gleser, H. Nanda, and N. Rajaratnam, *The Dependability of Behavioral Measurements: Theory of Generalizability for Scores and Profiles* (New York: Wiley, 1972).

Cronbach, L.J., N. Rajaratnam, and G.C. Gleser, "Theory of Generalizability: A Liberalization of Reliability Theory," *British Journal of Statistical Psychology*, 16 (1963), 137-163.

Eikeland, H-M., "The Structure of Generalizability Theory for Hierarchically Stratified Tests," unpublished report, University of Oslo, Norway, 1972.

_____, "Generalizability Estimates for Difference Scores: An Aspect of the Construct Validity of Tests," unpublished report, University of Oslo, Norway, 1973.

Gleser, G.C., L.J. Cronbach, and N. Rajaratnam, "Generalizability of Scores Influenced by Multiple Sources of Variance," *Psychometrika*, 30 (1965), 395-418.

Hornke, L.F., "Antwortabhängige Testverfahren: Ein Neuartiger Ansatz psychologischen Testens," *Diagnostica*, 1 (1977), 1-14.

_____, "Computerunterstütztes Testen (CUT) von Prüfungsangst," *Zeitschrift für Differentielle und Diagnostische Psychologie*, 4 (1981), 325-335.

Mispelkamp, H. "Die Ableitung von Aufgaben des 'Textverstehens' mit Hilfe psycholinguistischer Ansätze," unpublished report, Universität Düsseldorf, West Germany, n.d.

Shavelson, R., and N. Webb, "Generalizability Theory: 1973-1980," *British Journal of Mathematical and Statistical Psychology*, 34 (1981), 133-166.

Wittman, W.W., "The Lack of Multivariate Approaches in Psychological Research With Special Consideration of the Interactionism Controversy," Research Report 5 (Psychological Institute, University of Freiburg, West Germany, July 1982).

_____, "Multivariate Reliability Theory: Principles of Symmetry and Successful Validation Strategies," in *Handbook of Multivariate Experimental Psychology*, ed. R.B. Cattell and J.R. Nesselroade, 2nd ed. (New York: Plenum, in press).

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Biological Sciences

BIOLOGY AT ETH-ZURICH: INSTITUTE FOR BIOTECHNOLOGY

by Claire E. Zomzely-Neurath. Dr. Zomzely-Neurath is the Liaison Scientist for Biochemistry, Neurosciences, and Molecular Biology in Europe and the Middle East for the Office of Naval Research's London Branch Office. She is on leave until July 1986 from her position as Director of Research, the Queen's Medical Center, Honolulu, Hawaii, and Professor of Biochemistry, University of Hawaii School of Medicine.

The Institute for Biotechnology of the Swiss Federal Institute of Technology (ETH-Zurich) is doing first-class work that is making important connections between basic and applied areas of biotechnology.

Background

In 1976, based on a proposal from the ETH president, Professor H. Ursprung, the institute's governing council resolved to promote biotechnology research in Switzerland. This resulted in the establishment of a technology-oriented division within what had been a purely academic biology faculty. At the time, this was considered a daring enterprise as very few similar organizations existed that could serve as models. What was known, however, was that the field of biology was constantly changing and that, in the future, applied biology would have a much greater range than ever before. Of the two Federal Institutes of Technology in Switzerland, only the one in Zurich had a well-developed biology department. Thus, this was the rationale for establishing biotechnology research at the ETH in Zurich.

From 1979 to 1980, the biotechnology group was located in small buildings in central Zurich, but in 1981 the group moved to a wing in the technical physics building located at Hönggerberg (a suburb of Zurich and the site of the satellite campus of the University of Zurich).

The Institute of Biotechnology was formally established on 1 January 1982. The research programs of this department were oriented toward a concept established in 1974-75: to determine the basics for the technical use of living

cells and their components and to further develop their possible applications. Besides microbes, the cells of higher organisms (plant and animal cells) would also be studied. The resulting strategy included the establishment of a pilot plant at Hönggerberg which would allow investigations in the development of bioreactors, scale-up of processes, process development, computer applications, and processing. Thus, pure biology was deliberately combined with technical methodology.

For a conceptual understanding of biotechnology, precise bioprocesses must be selected. Technological basics cannot be developed using incompletely investigated principles. A solid knowledge of the fundamentals of the function and control of living cells is essential. For this reason, further research in still-unexplored areas of biology is needed.

Since the establishment of the Institute for Biotechnology, the research organization of the institute has been developed to reflect the goals stated above (Table 1). Not only are requirements for scientific academic research considered, but also, as much as possible, the needs for technological applications. For example, extensive work with yeast has been undertaken to deal with its most important regulatory phenomenon--that is, to understand and eventually control the glucose effect. Years of work in this area have led to a new type of ethanol production, to process development with eukaryotes (single cell protein produced on sugar or hydrocarbons), to process development with prokaryotes (interferon production), and to joint industrial work in the development of biosurfactants. Research work on the microbial degradation of lignin could ultimately ensure a continuous supply of raw materials. Current research with thermophilic bacteria could reveal ways to produce materials with properties that are unknown today.

During the seventies, the picture of biotechnology changed dramatically. When work on antibiotic development dominated in the past, no one could predict how much genetic technology would change the future course of biotechnological production. Biotechnology-produced hormones, leukines, monoclonal antibodies, artificial intelligence, and bioswitches are, to a large extent, only catchwords today; tomorrow they may be reality. The progress made in biochemistry is impressive: gene synthesis, construction of cell-free functioning elements for the conversion of light into chemical energy, and the development of new types of measuring equipment and biotransformation have all been accomplished successfully. Not all that is possible is yet visible on the horizon; many more research projects are still to be formulated.

The following short descriptions of the most important projects currently being carried out by the institute indicate the many types of research work that have originated from the single basic concept of biotechnology.

New Biotechnological Processes Using Yeasts

The yeasts are the most important eukaryotic microorganisms, having diverse applications in both industry and research. Although these organisms have been used in biotechnological processes for centuries, their metabolism is not yet completely understood. However, through the use of genetic research,

Table 1

Organization of the Department of Biotechnology

Bioprocesses (Prof. A. Fiechter)	Enzyme Technology (Prof. K. Mosbach)	Wastewater Biology (Prof. G. Homer)
1. Mass cultivation of living cells	1. Enzymology	1. Water biology
2. Improvement of process kinetics	2. Immobilization of enzymes	2. Water pretreatment
3. Mass transfer	3. Alteration of enzymes	3. Sludge treatment
4. Scale-up	4. Process development	4. Biogas
5. Process development	5. Analytics	5. Thermophilic sludge treatment
6. Measurement & control	6. Clinical testing	
7. Computer applications		
8. Direct-digital-control strategy		

better knowledge of the yeast cell metabolism and potential applications will definitely lead to a better understanding of yeast processes and should reveal new kinds of possible uses for these organisms. At the institute, problems in yeast metabolism have been under investigation for many years. The following examples clearly demonstrate the important connection between basic research and technical applications.

Metabolic Regulation and Alcohol Production by Yeast Under Aerobic Conditions. Various yeasts show special metabolic characteristics--they produce alcohol when grown at high sugar concentrations and in the presence of oxygen. The causes and effects of this metabolism and influences on the metabolic regulation have been and still are subjects for scientific research. Knowledge gained from this research has led to the development of a new process for ethanol production under aerobic conditions. Briefly, the method consists of aerobic alcohol production with cell recycling. The efficiency of this production is improved through the recycling of producing yeast cells. The culture broth is removed from the bioreactor (developed at ETH), the cells are pelleted in a separator, and then the cells can be used again in the bioreactor. Thus, biomass concentrations of over 50 g/L can be obtained.

Occurrence and Regulation of Cytochrome P-450. Microorganisms that use water-insoluble hydrocarbons require a special oxidase system in which the water-insoluble substrate is converted to a water-soluble form so that it is accessible to the organisms. An essential component of this monooxygenase complex is cytochrome P-450. The following unique properties make this protein complex interesting for biotechnology research:

1. Human liver cells produce a large number of cytochrome P-450 isoenzymes, which play an important role in detoxification reactions. The basic molecular biology for the synthesis of this enzyme, however, is not yet known and is extremely difficult to study in liver cells.

2. With the transformation of water-insoluble organic material to water-soluble matter, the production of cancer-causing substances can take place. Exact knowledge of the substrates and of products of monooxygenase systems is therefore of great importance.

3. Monoxygenase can be of great technological use for the manufacture of biologically active substances for stereospecific biotransformation.

The work of the Institute for Biotechnology is directed toward the characterization of cytochrome P-450-containing systems in yeasts. These organisms are eukaryotic, living cells that can be grown by simple operations and are easily accessible for genetic manipulation. The long-term goal of this research is the large-scale production of monooxygenase, a prerequisite for technical applications.

Production of Microbial Surfactants

There are various uses for surface-active agents (surfactants). Each year, several million tons of synthetically produced surfactants are used worldwide as food additives, as detergents, in cosmetic products, and in many industrial processes. The demand for surfactants is expected to become even greater in the future, especially if they prove of value in tertiary oil recovery from reservoirs, tar sands, or oil shale. However, the use of synthetically produced surfactants is not problem-free. Their production is very expensive, and severe environmental pollution problems have been attributed to the use of these heavily degrading materials.

One solution to this situation--the increasing demand for surfactants on the one hand and environmental problems on the other--can be the use of surfactants that are produced biologically, called "biosurfactants." It has been known for a long time that some microorganisms produce surface-active agents, which allow the organisms to grow on water-insoluble substrates. However, for many years the interest in these microorganisms and their surfactants was only an academic one. Today, effective research of possible biosurfactant applications is now taking place.

Biosurfactants have a variety of molecular structures. One example is a rhamnolipid surfactant obtained from bacteria. The surface-active property is due to the polarity of the molecules, which results from the lipophilic fatty acid group on one end of the molecule and the hydrophilic sugar portion at the other end. The production of microbial biosurfactants occurs under extremely heavy foam conditions. This foam cannot be controlled in the conventional stirring vessel. However, the scientists in the institute have developed a type of bioreactor which can break down foam and thus have overcome the problem of foam formation.

The present research work at the institute consists of: (1) a search for

microorganisms that secrete surface-active agents; (2) isolation and characterization of biosurfactants; (3) optimization of the production of biosurfactants; (4) testing of biosurfactants for possible use in oil recovery, in cosmetic production, or as food additives; (5) development of production processes in the laboratory; (6) scale-up of the processes for biosurfactant production; and (7) production improvement through genetic manipulation of the surfactant-producing microorganisms.

Biological Degradation of Lignin

Lignin, a polymer of aromatic compounds produced by plants, makes the structural matter of roots, stems, trunks, and limbs resistant to certain chemical, physical, and biological effects. At least 35 percent of the walls of plant cells, where the structural material is formed, is composed of lignin. Most of the rest of the cell walls consist of the polymer compounds cellulose and hemicellulose, which also contain some lignin. One can speak of this relationship as the lignification of plant-like material.

After the lignin has been extracted, two of the uses for lignin-containing biomass are as raw material for cellulose production or for sugars that can be used further. Today, lignin extraction takes place exclusively with the use of chemical and physical methods which consume a great deal of energy, require a large amount of chemicals, and produce environment-polluting wastewater. The extracted lignin is usually burned.

Since lignin is degraded by microorganisms in nature, it would seem possible to accomplish industrial detoxification using biological rather than chemical methods. In this process, the microbial bleaching of cellulose or the production of basic aromatic chemicals from lignin-containing wastes could take place. However, for an economical detoxification process, more research on its microbial, physiological, and biochemical aspects is needed to determine optimal conditions for lignin degradation and degradation methods. The long-range objective of this work by the institute is to determine practical and economical ways of influencing this lignin degradation process. The complex structure of lignin molecules has already required very time-consuming investigation by these scientists. Thus, quick success in this area cannot be expected. However, some progress has already been made. For example, straw, a widely known waste product, consists principally of lignin, hemocellulose, and cellulose. The former two compounds can be extracted with sodium hydroxide, and the remaining residue, which consists of pure cellulose tissue, can now be degraded microbially. In addition, the fungus *Phanaerochacte chryposporium*, which can degrade lignin (albeit very slowly in nature), has been used in special mass-cultivation techniques developed by these scientists (nitrogen limitation, optimization of oxygen supply, etc.). The resulting degradation rate is 10 times faster than previously reported rates.

Bioprocesses With Thermophilic Microorganisms

During the last decade, there has been tremendous interest by industry in thermophilic microorganisms. When compared with the mesophilic organisms used in industry today, there are several advantages of thermophilic microorganisms:

1. These organisms grow and produce metabolites faster than mesophilic ones; faster growth naturally means higher productivities and the need for smaller production units.
2. At high temperatures, the cells and products (especially enzymes) of thermophilic microorganisms are also stable and active (for example, protease in detergents).
3. Thermophilic microorganisms have very high minimal growth temperature (usually higher than 40°C) and therefore are not pathogenic, which substantially facilitates work with these cells.

Before successful industrial use of thermophilic microorganisms can occur, more essential basic research is necessary. Questions such as the following must be answered: What demands do thermophilic microorganisms make on cultivation media? What culture conditions must be followed in order to obtain the highest possible growth and production rates? What yields can be obtained, and what part of the substrate can be improved to enhance maintenance requirements?

With the continuous cultivation method used at the institute, many different kinds of thermophilic microorganisms have been and are being characterized and potentially useful enzymes (amylase, protease, oxido-reductase) can be further investigated. The results obtained thus far are very promising, according to these scientists, and have been so successful that generation times of less than 11 minutes have been obtained in the laboratory.

Some of the thermophilic organism studies at the institute include several strictly anaerobic organisms. The manipulation of these microorganisms requires special technical conditions, such as the elimination of oxygen using special equipment developed by members of the department. Indeed, the method of obtaining high growth rates using thermophilic microorganisms brings many technical problems along with it. This requires that more care be given to the type of equipment used in thermophilic processes than is needed in growth experiments with mesophilic organisms. These problems are also being studied in the institute.

Control of Bioprocesses

The critical requirement for the efficiency of a biotechnological process is control with respect to the biotechnological characteristics of the process. Measuring and regulating a microbial process can be difficult. In multiphase systems, all relevant parameters must be measured under sterile conditions, and inaccurate measurements caused by wall growth on sensors or disturbances due to foam formulation must be prevented. Process regulation should be suitable for both maximum dynamic processes (consisting of seconds), as well as for very slow process behavior (consisting of weeks).

The weakest link in the chain of process controls is the measuring technique; of course, certain physical and chemical dimensions can be measured *in situ* without difficulty (temperature, pH value, pressure, redox potential, etc.). However, other parameters of interest--the biological ones--are more difficult to measure (biomass concentration, metabolites, substrates, products). At the institute, two initial steps have been taken to solve this problem. The first step aims to solve the basic problem through development of new measurement sensors such as alcohol probes, carbon dioxide probes, and fluorescence probes for measurement of *NADH* concentration. The second step is the development of mathematical models for determining parameters that are not measurable.

The amount of data available from a biotechnological process is enormous and cannot be accurately determined using conventional methods. However, with the advantages available through electronic technology, this goal is feasible. At the Institute for Biotechnology, computers coupled on-line to bioreactors allow the accurate recording of data and efficient process control. In addition, they allow an on-going calculation of biological parameters, thus making possible the determination of control strategies based on actual biological quantities.

Biotechnology Pilot Plant

The biotechnology pilot plant is an important connecting link between laboratory and industrial-scale production. Bioreactors with a working volume of up to 3000 L make possible industrial-scale testing of procedures developed in the laboratory, as well as the further development of small-scale production procedures. Thus, large mixtures of desired products can be produced for application or toxicology studies. The small-scale production of, for example, interferon or biosurfactants and the cultivation of various microorganisms are feasible in this pilot plant.

The basic tool for combining cultivation problems with research work is the bioreactor, the physical reservoir for the performance of biological reactions (Table 2). Its task is to adequately supply cells with nutrients and to maintain environmental conditions (pH value, temperature, current, etc.) that are favorable to product formation. The bioreactor must also prevent cultivation problems such as wall growth, foam formation, culture broth separation, contamination, and insufficient oxygen

Table 2

Bioreactors in the Biotechnology Pilot Plant

Type	Volume	Remarks
Stirred tank reactor	30 L, 300 L, 3000 L	Classic reactor type
Airlift loop reactor	2500 L	Airlift reactor type; space saving
Propeller loop reactor	50 L, 600 L	Completely filled reactor; inhibits foam formation; prevents wall growth
Horizontal loop reactor	100 L, 1000 L	Completely filled reactor; prevents wall growth

supply. All of these requirements have been met by various models of bioreactors. In the pilot plant at the institute, the reactor models used for investigations are the classic stirred tank reactor and three loop reactors developed by different departments at ETH-Zurich.

Conclusion

The Institute for Biotechnology, in addition to a staff of excellent scientists, has first-class facilities for biotechnology research combining basic and applied research. The institute is funded primarily by the Swiss government but also receives some money from industry. The graduate students and post-doctoral fellows in the department are not only from Switzerland, but also from other European countries and the US. In addition to the Institute for Biotechnology, the Institutes for Molecular Biology-Biophysics, Molecular Biology, and Cell Biology are also located at ETH-Zurich. There is extensive interaction between members of these departments, so that each can take advantage of the specialized techniques of other departments--for example, the genetic engineering methods of the molecular biology institute.

A description of the research of the molecular biology-biophysics and molecular biology institutes will be presented in the following articles. Dr. Thomas Rozzell discusses the research of the Institute for Cell Biology in the article beginning on page 307.

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BIOLOGY AT ETH-ZURICH: MOLECULAR BIOLOGY AND BIOPHYSICS

by Claire E. Zomzely-Neurath.

ETH-Zurich's Institute for Molecular Biology and Biophysics and Institute for Molecular Biology I do first-rate research with relatively small staffs. This article looks in detail at innovative work in areas such as neuropeptides and hormones, protein structure and enzymology, gene functions, interferon, and molecular virology.

The Institute for Molecular Biology and Biophysics

The research carried out at the institute covers a wide range of projects within the context of molecular biology and biophysics. The emphasis is on basic research in the following areas: (1) the mechanism of transmission of information mediated by neuropeptides and peptide hormones; (2) chemistry and physics of peptides; (3) methods for the synthesis of peptides and nucleic acids; (4) structure-function studies of macromolecules; and (5) biocatalysts. Several of these research projects are described below.

Neuropeptide and Hormones Research Project. This research group continues the pioneering Swiss work that led to the founding of the Institute for Molecular Biology and Biophysics. Some of this research included the development of new chemical methods that made possible the first syntheses of complicated antibiotic and hormonally effective compounds and peptides with ring-like and linear structures such as Gramacidin S, Angiotensin I and II, α and β melanotropin and adrenocorticotropin (ACTH). Many patents and economically important products for medicine--e.g. ACTH and Synthaten--attest to the importance of basic research in the field of peptides.

The interest of this group has expanded from synthetic methods to the exploration of the mechanism of transmission of information via neuropeptides and peptide hormones. Knowledge of the mechanisms involved at the molecular level is of significant scientific and practical value. Research during the past few years has led to a merging of the fields of endocrinology and neurobiology. It is now known that many peptides (more than 30) occur in both systems together. These peptides are produced by endocrine glands as well as in the central nervous system (CNS) and can act as hormones, neurotransmitters, and neuromodulators. Peptides are considered today to be some of the most important regulatory molecules of the body. They transmit, in unimaginably small amounts, life-important information from one cell to another as well as from one part of the body to another. Recent research also implicates peptides in the effects of acupuncture. Their role in certain behavioral effects--for example, angiotensin in thirst-conditioned behavior of birds, fishes, and mammals--has been firmly established. ACTH derivatives appear to facilitate attention and memory, especially in aging persons; and endorphins have been implicated in emotional well-being. Thus R. Schwyzer and his coworkers postulate that information about the functions of peptides can provide a clue to the understanding of psychosomatic events.

The basic questions being investigated by Schwyzer et al. are: (1) how

is the information which is being transmitted from the "sending cells" to the "receiving cells" locked up in the peptide molecules, and (2) how is it being read out? Definitive answers to these questions afford the possibility of more effective applied research and the development of drugs or methods to alleviate and/or cure behavioral and emotional disturbances.

Neuropeptides and peptide hormones typically consist of a chain of between five and 50 amino acids. There are 20 different amino acids--i.e., "commands" for the release of certain effects and "addresses" which lead the peptide to the correct reading-out mechanism in the correct receiver cell. Their concept includes the presence of receptors on the surface of receptor cells, and evidence for these receptors has already been obtained. Each receptor recognizes specifically only one kind of peptide and reacts only with the specific peptide in order to release the respective effect in the receiver cell. The necessary peptide-receptor mutual effect consists theoretically in a mutual "complementary" attachment to the molecular surfaces. The receptors appear to be large, relatively rigid proteins which are present only in small amounts. Schwyzer et al. have found that most of the neuropeptides and peptide hormones are very mobile, filiform molecules which also occur in only a small amount in the blood or in the intercellular fluid. Theoretically, it is thus possible for interaction to take place in the short time necessary for regulatory processes. The question posed by these investigators is that of the molecular mechanisms responsible for peptide regulatory effects.

Schwyzer et al. have found that the cell membrane acts as a catalyst for the transmission of information. They have shown that the extremely thin lipid membrane which envelopes the living cells and in which the receptors are imbedded "catches" neuropeptides and peptide-hormones like an antenna and leads them quickly to the receptors. The flexible peptides become folded and oriented in the membrane so that the "command words" are presented to the receptors in a form and position which make possible a fast, unmistakable recognition and subsequent reaction. The "address" reacts with the membrane surface so that the command can react only with certain receptors. Their model can explain what structural entities of the peptides are preferred by certain receptors in order to accomplish specific biological effects. Thus, new approaches can be devised for the investigation of faulty molecular conditions which can be manifested as receptor-caused diseases such as certain forms of diabetes. Schwyzer et al. postulate that drug addiction may have a connection with the peptide-receptor hypothesis in that drugs similar to some of the peptides will bind to certain receptors.

Other studies of the neuropeptide and hormone research group are concerned with the investigation of receptors themselves as well as with the development of new chemical methods to produce drugs which can be applied to peptides as well as to nucleic acids. Since receptors, compared with many other substances of an organism, occur in extremely small amounts, it takes unusual methods to examine them. Schwyzer et al. have coupled neuropeptides to a virus, the tobacco mosaic virus. These virus conjugates act as "super hormones"--i.e., they have an enhanced biological effect. In addition, this group has developed new methods for the synthesis of peptides and nucleic acids which are being used in their studies.

Protein Structure and Enzymology. This research group, headed by H. Zuber, deals with the relations between structure and effect of proteins. All life processes (cell metabolism, the functions of organs and organisms) are based on the activity of protein molecules.

The basic units of protein are large molecules, polypeptides biosynthetically produced in nature by the synthesis of long-chain amino acids (polymers with 100 to 500 amino acid units). The sequence of the amino acids in these polymer chains determines the arrangement in space (folding, conformation) of these amino acid chains. The folded amino acid chains can be combined further into larger molecules (polypeptides or protein complexes containing up to 100,000 amino acids). The arrangement in space of the amino acid chains and the form of the polypeptide or protein complexes determine the biological activity of the protein molecule. The research of Zuber et al. is concentrated on the explanation and the understanding of the biological activity of the proteins on the basis of their chemical and spatial (i.e., molecular) structure. It is essentially basic research. Zuber considers that all basic research as well as applied research (medicine, biotechnology, energy research in biology) are and will be based on the results of research such as his in the framework of the biological activity and the molecular structure of proteins--i.e., structure-function relationships.

Zuber's group is also investigating thermophilic, mesophilic, and psychrophilic enzymes with respect to

temperature adaptation and energy transduction. Thermophilic enzymes are biologically active at high temperature, up to 100°C, mesophilic enzymes at 30°C to 40°C, and psychrophilic enzymes at low temperature (0°C to 30°C). The aim of this research group is to obtain insight into the biological activity of enzymes (proteins) and their molecular structure at various temperatures. These studies are important for two reasons:

1. One can obtain fundamental information on the thermostability of protein structures and activity in cell metabolism of proteins in order to understand at a molecular level the structural and functional adaptability of the organism.
2. The comparison of thermophilic, mesophilic, and psychrophic proteins (enzymes) furnishes new information about the principles of the thermostability of the proteins and protein dynamics that are of importance for biological activity.

Zuber et al. are comparing the structure and function (activity) of enzymes adapted to various temperatures--e.g., lactic acid dehydrogenases from bacteria. These investigators have found differences in the spatial and chemical structure of these enzymes that could be related to their quality (thermostability, protein dynamics, biological activity). The data obtained are being used for goal-oriented variation of enzymes (protein structure) with respect to stability and activity (catalytic activity and substrate specificity). This is of special interest for the biotechnological application of enzymes for applied research, including the improvement and adaptation of enzymes for industrial purposes. The studies on temperature adaptation of the enzymes (proteins) provide data and an increased understanding of the energetics of enzyme catalysis on the basis of energy transduction--the main goal of these researchers. The fact that adaptation of enzyme structure to temperature (during the development of organisms over millions of years)--while at the same time and reciprocally the thermostability and catalyic activity have been varied (an increase in thermostability results in the lowering of catalyic activity and vice versa)--points to an adaptation of the conformational state of the enzyme molecule with respect to the energetics of catalysis.

Biophysics Research Project. K. Würtrich and his group deal with the theme of spatial structure and internal mobility of biological macromolecules in solution. They primarily use nuclear magnetic resonance (NMR) methods for their studies. In particular they make use of two-dimensional NMR, a technique developed at the ETH-Zurich: Biological macromolecules (nucleic acids, proteins, etc.) fulfill central functions in all biological processes. The role of the action of nucleic acids (DNA, RNA) and proteins (enzymes, hormones) depends primarily on their spatial structure.

Furthermore, it is essential for the function of many biological macromolecules that they possess a certain mobility. For example, enzymes (biocatalysts) for the degradation of foodstuffs and proteins have to adapt themselves to the reaction molecules in a structural manner and, during the enzymatic reaction, must exert certain movements. Until recently, knowledge about the spatial structure of proteins and nucleic acids had been obtained by x-ray structural analysis which required these macromolecules to be in a crystalline form. However, proteins and nucleic acids fulfill their biological functions almost exclusively in solution. The systemic application of NMR methods to structural problems has been developed during the past few years by this research group, initially to determine the spatial structure of small proteins in solution so that one is dealing with the molecule in a fluid environment more natural than the rigid structure of the crystalline form. Internal motility of the molecules is manifested in many aspects of the NMR spectra. Würtrich et al. are now also applying their NMR method to an examination of larger proteins as well as to DNA fragments (synthesized by the group) and their complexes with proteins or pharmaceutical agents (e.g., anticancer drugs). These researchers consider that the information obtained by their methods can lead to a better understanding of the mode of action of certain drugs.

Institute for Molecular Biology I (Chemical-Genetic)

This institute, headed by C. Weissmann, has 40 members, including scientific and technical staff as well as graduate students and research fellows. The research projects deal principally with the examination of structure and function mechanisms of genetic material. The ultimate goal is to use the information obtained from this research for biotechnological purposes. The projects are subdivided into three categories: (1) mechanisms of gene function, (2) interferon research, and (3) molecular

virology. These research projects are presented below.

Mechanism of Gene Function. The genetic information contained in the chromosomes of the cells of organisms determines the chemical and biological qualities of all living entities. The genetic information is localized in DNA, which is present in the nucleus of every cell. The DNA constitutes the molecular "language," the so-called genetic code, which is essentially the same for all known living organisms and was deciphered 20 years ago. DNA consists of a sequence of four different building blocks, the deoxyribonucleotides. The transformation of the genetic information into cellular activities--i.e., gene expression--takes place in two steps:

1. Transcription: in the cell nucleus individual genes whose activity is required by the cell create short-lived usable copies called messenger RNA (mRNA). They are written in the same language as the gene itself but consist of building blocks that are slightly different chemically, the ribonucleotides. The mRNA is transported from the cell nucleus to the cytoplasm, where the proper evaluation of the genetic information takes place.

2. Translation: the information coded in the mRNA is read out via the protein synthesis apparatus (ribosomes), which builds up the cellular proteins under the direction of the mRNA. Proteins are made up of amino acids, and their sequence determines the spatial structure and thereby the multiple biological activities of the proteins, which are essential for the formation and the metabolism of the cell as well as the total organism.

As mentioned above, the information encoded in a gene must first be transcribed into mRNA. Several years ago it was found that the primary copy of the gene (primary transcript or pre-mRNA) had to be modified before it could be used for the synthesis of proteins. In many cases, certain "introns" have to be cut out of the primary transcript of the genes of higher organisms, a process called splicing. This process has to be carried out with the greatest precision, and the question arose as to how the places where the pre-mRNA cuts occur are marked. C. Weissmann and his group have carried out extensive research in this area. Using genetic methods they effected the exchange of certain building blocks (nucleotides) of a nucleic acid (i.e., goal-oriented mutagenesis). Each nucleotide at the place of splicing is specifically exchanged, and then one ascertains whether recognition of the splicing domain is prevented. In this way, these investigators were able to determine the recognition signals. At present this group is dealing with the mechanism which underlies the splicing process.

Weissmann et al. are also investigating the regulation of gene expression. The quantity of a protein synthesized in the cell can be controlled directly or indirectly in several places. For example, the synthesis of mRNA can be impeded or increased, which in turn determines the extent of protein synthesis. Other influences on protein synthesis are the decrease or the maturation of mRNA as well as the reading out (translation) of mRNA at the ribosome level. Most of the genes of a particular cell are inactive because many proteins are cell-specific and are produced only in a specific cell type (e.g., hemoglobin in red blood cells). Other genes become activated when needed. For example, the synthesis of metallothionein (a protein able to bind heavy metals) is activated when heavy metals are administered or ingested. Another example is interferon. This protein, which exhibits antiviral activity, is synthesized only when a cell is invaded by a virus.

Interferon Research. Weissmann et al. have been studying how the synthesis of interferon and other proteins is regulated. They have shown in the case of interferon that mRNA synthesis (transcription) is normally impeded and is only activated if a virus invades a cell. Further examination of the interferon gene revealed that a region in the vicinity of the gene is responsible for the control of transcription. This was demonstrated using gene technology. If the respective DNA promoter was separated from the interferon genes, transcription of the gene after viral infection did not take place. Also, it was possible to couple the interferon promoter to a totally different gene, the globin gene. Then the globin gene was subjected to the same control as was the interferon gene. It was activated only after a viral infection. The exact structure of the interferon promoter is now established, and it only remains to determine which signals, after viral injection of a cell, act on the interferon promoter to activate it.

Interferon was discovered by A. Issacs and J. Lindemann in 1957. They found that cells treated with inactivated flu virus secreted a substance which protected untreated cells from a subsequent viral infection. Interferon was

subsequently found in a variety of vertebrates ranging from fish to human. Interferon plays an important role in the body's natural defense against viruses. While the known, traditional immunizing substances protect only against a particular viral family or disease, interferon is effective against a wide variety of viruses. Besides this antiviral effect, interferon also has a growth-retarding effect and influences immunological events by increasing the activity of the defense cells (lymphocytes and macrophages). These qualities form the basis for possible uses of interferon as an antiviral and antitumor agent. Although interferon exhibits a very high specific biological activity, it is produced in the body only in very limited amounts. After a viral infection, there is only one-millionth of a gram of interferon in human blood. Likewise, the exploitation of interferon from cell cultures stimulated to produce it by viral injection is difficult because of the small amount.

In order to obtain better insight into the structure and function of interferon, Weissmann and his group worked extensively on the isolation of interferon genes and expression of the gene as the protein product. They were successful in this research and were the first research group to clone and express interferon using recombinant DNA techniques. Also, using the interferon DNA they isolated, Weissmann et al. were able to isolate all interferon genes from human chromosomal DNA. They found that leukocyte interferon was coded not by one, but by at least 14 different but closely related genes. The amino acid sequence derived from the nucleotide sequence showed that the various types of leukocyte-interferon all possessed a similar structure but still showed some specific differences.

Weissmann et al. have also been working on producing relatively large amounts of interferon using gene-technology methods in order to have sufficient material for testing the antiviral and antitumor effect of interferon in human subjects. In order to examine these and many other biological activities of interferon, milligram to gram amounts are needed. To achieve an increased production of interferon, these investigators replaced the interferon promoter with the promoter of a bacterial gene. In this way, they were able to achieve a high expression of the interferon gene in *E. coli*. In contrast to cell cultures, bacteria can be grown cheaply, quickly, and in large amounts. The modified *E. coli* is grown in large fermenters yielding several milligrams of interferon per liter of bacterial culture and resulting in the production of interferon in gram quantities. Using classical biological cleansing procedures, one can obtain a highly purified product that can be crystallized. At the present time, Weissmann et al. are able to produce 100 mg (and more) of interferon per liter of bacterial culture. In the best cultures, up to 40 percent of the protein mass consists of interferon.

Although *E. coli* is often very useful for the microbiological production of proteins, it is often not very useful for the synthesis of proteins from animal cells, especially if one deals with modified proteins such as glycoproteins. This applies to interferons β and α, which contain sugar residues. Therefore, Weissmann and his group have programmed animal tissue culture cells using gene technology so that a specific protein is synthesized and excreted into the medium in appreciable amounts. In this case, the interferon gene was introduced into animal cells coupled to a "strong" viral promoter so that these cells produced interferon without viral infection. In order to increase production, the number of copies of the introduced gene can be increased by certain artificial means.

Gene-technology methods can also be used to produce deliberately modified proteins that do not occur in nature. Such modified proteins--for example, modified interferons--are of value in obtaining information about their mode of action during examination of their biological activities. For this purpose, Weissmann and his group have developed a whole arsenal of gene technological methods that allow the modification of genes in a goal-oriented manner so that bacteria then make proteins with the desired structural change (goal-oriented mutagenesis). One of the current projects has as its goal to define the loci necessary for the biological effect of interferon by changing certain amino acids at different places in the interferon molecule. Furthermore, these investigators are trying to shorten the protein chain of the interferon molecule from both ends in order to define the minimal length of a still-active interferon protein. Another possibility being developed consists of making interferon proteins by using natural gene recombination mechanisms from two different interferon-type hybrids--i.e., mixed interferon genes. The various interferons possess various activities on other-than-human cells, for example, on mouse cells. By determining the activity of these hybrid interferons on cells of different organisms, those parts of interferon molecules can be

defined which are responsible for the cell specificity.

Molecular Virology. Viruses are not living organisms. The replication of their genome and the expression of the genetic information contained therein can only occur in living hosts. Viruses are hangers-on at the molecular level. They use the mechanism which the cell uses for the replication and expression of its own genetic material. Since the genetic material of even complicated viruses is simple in comparison with that of a cell, the examination of viruses and their multiplication can be used to understand better the replication and expression of the genetic material of bacterial and of higher organisms. The genomes of viruses consist either of DNA or RNA. Most of the viral diseases in man and animal, and especially in plants, are caused by RNA viruses. Although the various kinds of RNA viruses follow several modes in their multiplication, one feature is common to all: they have to cause the synthesis of enzymes which enable their RNA to multiply. This is necessary because the host cell, which copies its RNA from the DNA, does not contain any RNA-copying enzymes.

Weissmann and his group have been studying bacterial and animal RNA viruses. The relatively simply structured Qβ RNA virus which multiplies in the human intestinal *E. coli* bacterium is especially suitable for the study of viral RNA replication. It is the only virus whose RNA can be multiplied a thousandfold in the test tube by the use of a highly purified enzyme isolated from Qβ-infected bacteria. This enzyme, which can copy the viral RNA strand within 100 seconds, is highly specific. Only viral RNA is recognized and replicated but not the approximately 1000 different kinds of RNA of the host cell. The specific recognition mechanism has only been partly clarified. However, it is known that not only the ends of the RNA molecule (where the copying begins) but also regions of the interior are recognized by this enzyme. In order to elucidate the functions of the different Qβ-RNA sections, a DNA copy (Qβ complementary DNA or cDNA) of the genome was prepared and introduced into DNA molecules capable of multiplication (so-called expression plasmids). Such viral cDNA-containing plasmids can be introduced into *E. coli*, where they will multiply. By certain tricks, the bacteria can be induced to produce viral RNA copies, which are packaged into viruses and released. Thus, it is now possible to change Qβ-cDNA by means of goal-oriented mutations of various kinds. Specific nucleotides or whole regions can be modified, eliminated, or newly introduced. According to the changes in cDNA, either functional viruses or non-functioning ones and viral proteins are produced. With such experiments in the living cell, the functional significance of specific viral RNA regions or viral proteins can be examined. However, a definitive statement about the interaction between RNA on the one hand and proteins on the other at the molecular level cannot be made with this method. Recently, however, Weissmann et al. have developed a system which allows practically any RNA segment to produce appreciable amounts of RNA in the test tube. Thus, the possibility exists of producing at will, changed viral RNA or parts of RNA and to examine the interaction of these molecules with purified Qβ replicas or other viral or cellular proteins by chemical and physical means.

Weissmann and his group are also studying the human measles virus. This virus, which invades human cells, has a complex organization. Its genome consists of a single RNA molecule which is about three times longer than that of the Qβ viral RNA. Its multiplication strategy is also different. The RNA is not replicative; rather, six partial copies are made which serve as mRNA, whose function is to control the synthesis of viral proteins. The structure of the measles virus RNA is known only roughly--in part because it is available only in small amounts and also because it is difficult to make complete cDNA copies. At any rate, the shorter cDNA copies obtained thus far, which contain nucleotide sequences of all six viral genes, have been useful as agents for finding the various viral mRNA species in infected cells. These results are important because the measles virus causes not only the well-known children's disease with its skin rash, but can also lead to a latent and long-lasting infection.

A typical example of the latter, fortunately occurring only rarely, is subacute schlerosing panenciphalitis (SSPE) a fatal disease of the brain that can occur 5 to 10 years after a measles infection. In the diseased brain cells one finds measles virus proteins and sometimes also virus particles. With the aid of the above-mentioned measles cDNA and specific antibodies, the brains of people who had died of SSPE were examined. It was found that in every case some of the viral components (mRNA species and viral proteins) were made normally, but others were not or were present in abnormal forms. In no two cases was the same picture observed. A

persistent viral infection is characterized by mutations in the viral RNA which occur during the course of multiplication in a cell and which destroy some viral function causing the cells to be chronically infected. Without really dying, the viral RNA seems to be transferred from cell to cell without forming infectious viruses which can be attacked by the immune defenses of the body. Multiple sclerosis has also been linked repeatedly with persistent measles virus infection. However, Weissmann and his group examined a number of cases using measles cDNA probes but were unable to find measles virus RNA. They consider, therefore, that there is no basis for the assumption that multiple sclerosis is caused by measles virus.

Weissmann et al. are also investigating scrapie, an infectious disease in sheep; its cause is still unknown. Scrapie resembles human diseases, such as Kuru or Kreutzfeld-Jacob disease, and is more accessible for experimentation--especially since it can be transferred to hamsters and mice. In collaboration with S. Prusiner (University of California Medical School, San Francisco), Weissmann and his group have examined scrapie-diseased hamsters and found a protein (PrP) in the brain which was augmented. These protein preparations are infectious--i.e., introduction into normal hamster brain leads to disease. The researchers examined whether this infectivity was caused by the protein itself (an unconventional explanation proposed some time ago), or whether a virus present in very small amounts or a viroid (a disease-causing nucleic acid) is responsible for the disease. In order to elucidate this question, the gene coding for PrP was isolated through cloning so that PrP could be produced without using infected animals and its infectivity was able to be proven. At the same time these investigators are continuing their search for a virus or viroid.

Conclusion

The Institute for Molecular Biology and Biophysics and the Institute for Molecular Biology I (chemical-genetic) are engaged in innovative and productive research of the highest quality. Each institute has a relatively small staff compared with comparable molecular biology institutions in the US. The policy of these institutes is to encourage interaction among the scientists and to foster interdisciplinary working groups. The success of this concept is evidenced by the large number of pupils and former staff scientists, many of whom are hired on a temporary basis of 3 to 5 years, who have carried out significant research and have attained recognition as professors in academia or as researchers in industry, both in Switzerland and abroad. These institutes have achieved international reputations for excellence in research. Many of the discoveries of these institutes have been patented since there are potential applications to various human diseases.

3/15/85

BIOLOGY AT ETH-ZURICH: INSTITUTE FOR MOLECULAR BIOLOGY II

by Claire E. Zomzely-Neurath.

The goal of the research projects at the Institute for Molecular Biology II is to understand the planning and directions of the genetic material that determines the biological processes of the organism. This genetically oriented molecular biology research is of tremendous importance since the genetic information contained in perhaps 100,000 different factors regulates in all organisms development, metabolism, propagation, aging--and even certain basic patterns of behavior.

M. Birnstiel, the director of the institute, and his colleagues have been at the forefront of research in the use of molecular biological techniques for studies of the complex events that take place in the cell at the molecular level. The research approaches at this institute are innovative and of top quality.

Birnstiel's staff consists of three senior scientists and 10 assistants as well as 17 students. The research group is international as many of the members come from other European countries as well as the US. This research group is relatively small compared with similar molecular biology institutes in the US. However, the creativity of Birnstiel and his group attest to the fact that ideas are of primary importance in research.

The questions posed by Birnstiel and his colleagues are: (1) how is it that out of one egg cell so many different cells are made; (2) how does every cell know exactly what it is supposed to do; and (3) what are the instructions which cause an immune globulin gene to be active only in B-lymphocytes?

Another way of posing these questions is to ask how the cell manages to produce the correct copies of the

genetic information--i.e., messenger RNA (mRNA)--in the correct tissue. We know today that the synthesis of a specific mRNA can only be started if some proteins which themselves are products of former gene activity build sequences on DNA and thereby determine the beginning and sometimes also the end of the DNA segments which can be read out. Once the primary copy is made, this must then be modified to yield the final mRNA. Only then can the cell use this mRNA as a template for the synthesis of proteins. Therefore, one asks at what places on the DNA is transcription initiated, and which principles guide the synthesis of the primary RNA copy. Birnstiel and his group consider that the first step for the solution of this question is structure analyses of the gene using modern gene-technology methods. To understand the underlying principles, however, one needs to use transformation experiments in which the isolated genes, either in their natural form or after goal-directed variation of the sequence of the four basic building blocks of DNA, are reintroduced into living cells of higher organisms. It may even be possible to produce whole organisms such as sea urchins and mice after injection of isolated genes into eggs and subsequent fertilization. In this way one can study the behavior of the returned genes in almost natural environments. One expects with such methods, following variation or removal of certain basic building blocks, to find specific defects in the gene activity and thereby to decipher the code of development-biological gene regulation.

Immunoglobin Gene

Birnstiel and the members of the institute are studying the activation of the immunoglobulin gene in B-lymphocytes. An immunoglobulin gene was produced in pure form by gene cloning. This gene represents only one-millionth of the total genetic information. These researchers posed the following questions: (1) can this isolated gene, if reintroduced into living cells, be expressed only in the "correct" cell type such as B-lymphocytes, or in all cell types; and (2) if a cell-specific expression is found, then through which DNA part of the gene is the cell specificity regulated?

A general problem in this experiment is the measurement of the activity of the reintroduced gene. If the introduced gene behaves properly, it will be active only in the predisposed cells; then it will simply produce a little more of the already existing gene product. In order to circumvent this difficulty, one takes a so-called test gene and couples it to the control elements of an isolated gene whose regulation one wants to explore--in this case the immune globulin gene. The test gene used for these experiments codes for the so-called A protein of a monkey virus. The immune globulin gene was cut into small parts using restriction enzymes. These single parts were coupled with the test gene, and these newly combined fractions were introduced into cells of various origins.

Birnstiel et al. found that only DNA molecules which contained, besides the test gene, a short DNA segment of immune globulin gene could lead to expression of the test gene, and this only at the right time--i.e., in B-lymphocytes and their derivatives. In this way, these researchers found, for the first time, a genetic element for the cell-specific expression of a gene. Thus, an important step was taken in the understanding of the division of tasks of the cells of higher organisms. Such small DNA functions are called "enhancers" and have been found in a series of genes in cells of higher organisms as well as in disease-causing substances such as viruses. For example, an enhancer segment of the insulin gene sees to it that this gene is activated exclusively in specific cells of the pancreas. The enhancer of the immune globulin gene was found to be located in the center of the gene (in an intron), and its location has provoked some interesting hypotheses about the sequence of the regulation cuts at the immune defenses.

Cell-type-specific enhancers are also responsible for the host area of a virus. The fact that the notorious AIDS virus prefers lymphocytes of the immune system probably has to do with a cell-specific enhancer, according to Birnstiel. It is also possible that enhancers are involved in cancer. It is known that sometimes in a viral infection an enhancer-containing part of a virus, in the neighborhood of a cell gene which regulates cell multiplication, becomes built in (proto-oncogene). In this way, this gene, directly or indirectly, is forced into activity without pause. This, in turn, leads to uncontrolled cell multiplications and finally to cancer. The proto-oncogene has become an oncogene by means of the enhancer. Such events have been documented in animals in cases of leukemias and breast cancer, and there are indications that such could also be the case in humans.

Histone Genes

Another study being actively pursued at this institute is the regulation

of the expression of the histone gene. Histones are structural proteins which are bound to DNA in a 1:1 relationship and are responsible for the packaging of DNA in the cell nucleus. The histone genes are interesting to study because their activity in the cell partition cycles is coordinated with DNA synthesis. On the other hand, they are also subject to developmental-biological regulation. This is most evident in the development of the sea urchin. In the first phase of cell division in an early sea urchin embryo, a whole battery of highly repetitive histone genes appear. After 12 hours these genes are inactivated, and their activity is replaced by histone genes of the gastrula type. Also, different histone genes are active in the sperm and egg.

Thus, there exists a developmental-biological repertoire of histone gene activity whose regulation Birnstiel et al. are examining. In every stage of development, there is ample biological material available which allows these investigators to isolate the regulatory factors which influence the histone genes. During the past few years, several histone genes have been systematically mutagenized. The injection of these histone gene mutants into the living cell nuclei of frog oocytes, followed by an analysis of the gene activity at the level of mRNA, has revealed a series of regulation signals at the beginning as well as at the end of histone genes. In a number of cases, the relevant regulatory proteins have also been detected.

Since the frog oocyte is a static cell system in which the exact contribution of the individual control elements to the expression of developmental state specificity is undetectable, Birnstiel et al. are presently reintroducing cloned and mutated histone genes into the egg cell of closely related sea urchins. In these experiments, miniscule amounts of these genes are injected into the sea urchin oocytes. After fertilization of the injected eggs, the embryos develop normally despite the biochemical intervention. The injected genes are then subjected to the developmental biological program described previously. Birnstiel et al. hope, by means of this experimental protocol, to identify those histone gene mutants that, because of certain structural changes, disturb the developmental biological behavior of genes.

Histone genes are subject, however, to the control of the cell-partition cycle. The multiplication of cells as found in embryonic development or in the growth of the organism, is, like all other biological functions, a precisely tuned event. The steering, and the process of cell multiplication itself, takes place in every cell in the same fashion and is delineated in the structure of the hereditary material. One assumes that in every phase of the cell cycle certain genes, whose products (certain protein molecules) could change the cells so that they go on to the next cell cycle, are turned off. This procedure is repeated several times and pushes the cells through the partition cycle. Also, in most simple systems, such as in yeast, at least 20 steering genes are required which, in part, control many other gene activities during the cell cycle. The most important studies in this aspect of research are the identification of the steering genes and also their action in conjunction with cell cycle-dependent genes. Such latter genes are, for example, the histone genes that are activated at the time of DNA synthesis and thereby make possible the building up of a new set of chromosomes in the partitioning cell.

In order to examine the cell cycle-dependent behavior of the histone genes, these researchers reintroduce a histone gene isolated from mouse as well as several mutants of the same gene into the cell of a particular cell culture line from mouse. These cells can be blocked on the basis of a genetic defect in that phase of the cell cycle that immediately precedes the DNA replication phase. If this block is removed, then all of the cells, all at the same time, go into the DNA replication phase. It is then possible to examine the activation of the histone gene which had been introduced exogenously. It appears that the regulation of the histone genes lies, on one hand, in the increased transcription of mRNA during the DNA replication phase and, on the other hand, in the diverse stabilities of the mRNA during the various cell cycle phases. These experiments have also shown that the posterior end of the mRNA molecule is responsible for its various stabilities. Therefore, the activity of histone genes can be regulated by means other than by changes in the transcription rate.

RNA Scripts

Birnstiel and his colleagues are also working on the RNA scripts (primary transcripts) of genes. Once a usable copy has been made by gene activity, additional steps determine if and how the primary transcripts are called upon for protein synthesis. It was shown that, in all cases, the end of the mRNA is chosen at the level of the primary transcript and not at the level of the

DNA. The completion of a correct end of mRNA is apparently very important for the translation of information from DNA to protein. If this process is missing, for example, in hemoglobin mRNA, thalassemia (a blood disease) results in humans. In order to ascertain the steering sequences that allow for initiation of the correct end of mRNA, these investigators inject precursor RNA molecules for the histone mRNA into the nuclei of living frog oocytes. The chemically unchanged precursor (primary transcript) is transformed, quickly and exactly, into a functional mRNA. With precursor molecules from which certain RNA sections were removed by chemical manipulation, it was possible to quickly identify the essential RNA signals. These are relatively short RNA segments (10 to 23 bases long) which frame the section sites on the precursor. How do these signals function? Further research revealed that the cell synthesizes special small RNA template molecules which correspond to the base alignment around the site of these sections like a mirror image and therefore fit on these (and only on these) base arrangements. One has to assume that, in further steps, an enzyme cuts through the RNA strand at the premarked site, once the templates are situated at the primary transcript. This seems to be a generally valid mechanism which has been preserved during evolution because, for example, human antiserum of patients who have the autoimmune disease lupus erythematosus can recognize sea urchin template RNA as an RNA-protein complex. Birnstiel et al. consider that the small RNA templates as well as the respective enzymes are products of earlier gene activities and they are now investigating this subject.

Birnstiel and his group are involved in basic research problems with the primary goal of understanding the complex events in a healthy cell. However, it has been shown in the past that some of the most important findings and developments with practical application have resulted from basic research. Therefore, these investigators believe that with the molecular biological approach they are using, it will be possible to develop new techniques to detect, for example, certain inherited diseases, degenerative signs of aging, and cancer, and to study and eventually cure these diseases by tailor-made, highly specific means.

Conclusion

The Institute of Molecular Biology II has been one of the pioneers in the use of molecular biological techniques for studies of the complex events that take place in the cell at the molecular level. The researchers have made major contributions to basic research and have achieved thereby an international reputation for excellence.

3/18/85

BIOLOGICAL ULTRASTRUCTURE RESEARCH AT ETH-ZURICH

by Thomas C. Rozzell. Dr. Rozzell is the Liaison Scientist for Biological Sciences in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on reassignment until August 1985 from the Office of Naval Research, Arlington, Virginia, where he is Program Manager for Bioelectromagnetics.

As can be inferred from the preceding articles, the Eidgenossichen Technischen Hochschule (ETH) in Zurich is a multifaceted research and teaching facility. I recently visited the Department of Cell Biology at ETH-Zurich and focused my attention on the research dealing with methods of preparing biological samples for electron microscopy studies of their ultrastructure. This research has received a lot of attention during the past few years as the areas of low-temperature and electron microscopy have gained momentum. The research is directed by Professor Hans Moor, a pioneer in the field.

This article will describe the technique of freeze-etching, which has been the focus of research in the Department of Cell Biology at ETH-Zurich for the past 25 years. Freeze-etching is one of the techniques vital to this emerging science and technology. I will attempt to show how Moor feels it can be used to improve our view of the fundamental building blocks that make up biological structures.

Background

During the past two to three decades, the electron microscope has become an extremely useful research instrument for biology and medicine. It permits the investigation of cellular and tissue components that are not visible with light microscopy and gives a view of substances down to macromolecular dimensions. The electron microscope is allowing us to close the gap between the molecular world and the world of the cell organelle.

However, the high resolution power of the electron microscope, which has

made this progress possible, brings with it special problems in sample preparation. The electron microscope only allows the examination of extremely thin (maximum of 0.0001-mm thick), completely dehydrated samples. This means that direct observation of live specimens is not possible. If cells and tissues are to be examined directly by the electron microscope, they must first be chemically stabilized, then dehydrated and embedded in plastic before being cut into very thin sections. Not only must these images be viewed with the electron microscope, they must somehow portray the actual structure of the subject as realistically as possible. The process of chemically fixing and embedding the specimen only fulfills these requirements to a certain extent because the specimen must, of necessity, be killed, and there is no way to avoid structural alterations. Many problems of interpretation thus arise, and there is often great debate as to which of the reproduced structures are natural and which are artificial. Furthermore, the electron beam of the microscope essentially destroys a biological sample prepared in this manner.

Over the years great strides have been made in chemical fixation and methods of embedding. These advances have not, however, eliminated the presence of artifacts. Attempts have been made to avoid some of the problems of freeze-drying and chemical fixation by the use of freeze-substitution, in which ice is withdrawn from the specimen by a solvent (alcohol or acetone) instead of by vacuum sublimation. It is usually necessary, however, to use a chemical fixative with the solvent to counter its harmful effects.

Freeze-Etching

In 1957, R.L. Steere in the US introduced a technique that essentially eliminated many of the disadvantages of freeze-drying and chemical fixation. It became known as freeze-etching. The freeze-etching technique is simply a method of producing a replica of a frozen specimen--by means of cutting, etching, and coating--and it is this replica that is investigated under the electron microscope. The preparation of the sample is such that the specimen is not subjected to either chemical or structural alteration. The Steere technique, as originally conceived, had a lot of problems and generally was applicable only to the narrow field of virology. It had great problems with reproducibility as well. Moor has spent approximately the last 25 years improving this technique and has brought it to the point where a major company (Balzers AG) has taken the initiative to develop the necessary apparatus to allow laboratories to carry out freeze-etching reliably and reproducibly. Much of Moor's improvements in the technique lie in the actual freezing stage.

Methodology

Freeze-etching consists of five steps, four of which are shown in Figure 1. These first four preparative steps are freezing, cutting, etching, and coating. The fifth step is the removal of the coating (replica) and viewing by the electron microscope.

Freezing. The purpose of freezing is to solidify the specimen in its natural state without causing changes in its structure or chemistry. The rate of freezing the sample is all-important and is one of the areas that Moor has advanced so admirably. In order to avoid the formation of ice crystals, the samples must be taken from 0 to -100°C in less than 0.01 seconds. This is equivalent to a freezing rate of 10,000°K per second. Some samples are actually taken to a temperature below -150°C. Moor has developed and is refining a new technique for freezing using a high-pressure propane jet as well as methods of measuring the temperature of the sample.

Cutting (also called fracturing). Once the specimen has been frozen, a very cold microtome knife is used to expose the inner surfaces of the specimen. The fracturing is carried out under very high vacuum and the part cut away disintegrates into very small pieces. The high vacuum prevents the cut surface from being covered with condensed moisture from the air. This must not be confused with the production of thin sections of material as might be used for preparation of light microscope slides or for examination of metals or plastics by the electron microscope. The fracturing is simply for the purpose of exposing a cut surface on the specimen frozen to the block.

Etching. The fracturing process that opens some of the structures in the specimen also exposes some ice which may obscure important details. The removal of this ice by vacuum sublimation is called etching. In this step, it is only necessary to remove the ice down to a depth of a few hundred angstroms in order to show fine structure in most specimens.

Coating. Next, the cut surface is coated with a very thin (approximately 25 angstroms) layer of an evaporated material. This is similar to making a mold or negative of the exposed surface which, after removal and cleaning, can

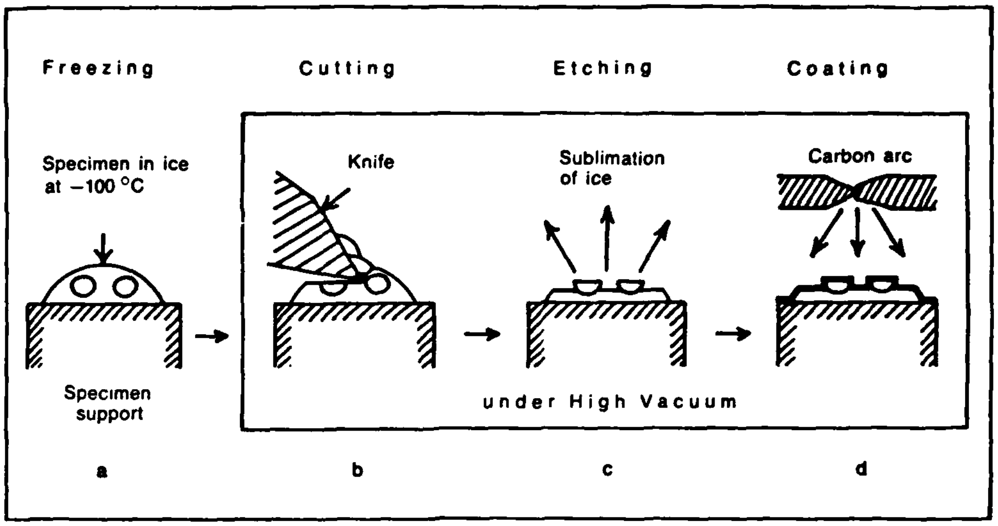

Figure 1. Four initial steps in the preparation of samples by freeze etching. (a) the object is frozen without artifacts by vitrification; (b) it is then cut or fractured under a high vacuum; (c) ice is sublimed from the cut surface; (d) production of a carbon replica of the specimen projecting from the etched surface.

be examined under the electron microscope. One technique that Moor and others have used involves depositing evaporated platinum and carbon on the cut surface. This mixture gives a replica that has essentially no surface features of its own and is insoluble, which allows the biological material to be dissolved away by solvents. The removal of the replica constitutes the fifth step in the freeze-etching process.

Release. After the replica is cast, it and the specimen are removed from the vacuum chamber, thawed, and floated on water. The adhering specimen is then removed using acids and caustic solvents. the cleaned replica is then placed on a specimen grid for examination in the electron microscope.

Applications

The pioneering work of Moor and his colleagues at ETH-Zurich and of others throughout Europe and North America is bringing new dimensions to the study of the ultrastructure of biological materials. Although structural details must still be discerned by inference, scientists such as anatomists, botanists, bacteriologists, pathologists, virologists, biophysicists, and zoologists all have a window into the cell and its components. While much can be learned about morphology and pathological changes, speculation must often remain about the function of different cellular structures. However, when techniques such as freeze-etching are combined with other techniques involving the live material, much of the uncertainty of speculation is removed.

Moor and his colleagues have shown that freeze-etching is a superior technique to chemical fixation and cryoprotection, and can give hitherto unknown details about fragile cells such as those comprising the nervous system. Moor says that freeze-etching allows the viewing of membrane fine structure because membranes can be fractured in such a manner that it breaks between the lipid bilayers.

Several investigators in Switzerland and in Germany are involved in complementary research, particularly involving vitrified water in biological specimens. There has been a lot of activity during the past few years in all areas of microscopy, but especially in electron microscopy and efforts to better resolve details of biological specimens in a state approaching the natural state. Moor feels that the next big breakthrough will come in the area of vitrification. This will lead to the solidification of a specimen in a microcrystalline state such that ice crystals never become larger than about 100 to 200 angstroms.

Moor and his colleagues are hoping to make new strides in improving the fracturing step and in improving the resolution through image processing techniques. At present, the ultimate

resolution is about 20 angstroms. They hope to get down to 10 angstroms. One of the apparent frustrations in this area lies in the fact that the electron microscope is capable of a resolution of 3 angstroms, yet the resolution of biological specimens is limited to more than 20 angstroms by the method of preparation of the samples. "It appears there is a lot more research to be done," says Moor.

4/19/85

ELECTROMAGNETIC COMPATIBILITY CONFERENCE FEATURES BIOLOGICAL INTERACTIONS

by Thomas C. Rozzell.

The Sixth Symposium and Technical Exhibition on Electromagnetic Compatibility was held from 5 through 7 March in Zurich, Switzerland. This meeting, organized by the Institute for Communication Technology of the Swiss Federal Institute of Technology, Zurich, was sponsored by the Swiss Electrotechnical Association. A large number of international groups cooperated with the sponsors and organizers in putting on the symposium. Among them was the Union de Radio Scientifique International (URSI), whose Working Group on Measurements Related to the Interaction of Electromagnetic Fields with Biological Systems, from Commission A, offered a workshop dealing with practical problems arising in quantifying the radio-frequency exposure of biological material. This article focuses on the presentations at that workshop.

Background

Electromagnetic compatibility (EMC) is a significant military and civilian problem, and one that is increasing annually as electronic systems become smaller and smaller, move closer together, and radiate more powerful signals. Radiated emissions of printed circuit boards, logic circuits, cables, etc., pose special problems in the design of naval vessels and aircraft. In general, little attention is given to interference with biological structures when electronic equipment is designed, the major emphasis being placed on achieving compatibility with other electronic equipment. While it is true that the signal sensitivity of electronic equipment appears to be greater than that of most highly organized biological structures, there is increasing evidence that sensitivities exist in biological systems that allow them to respond to extremely low intensities of electromagnetic fields. With this in mind, the EMC community is now beginning to address this issue, and the sessions at this symposium were designed to provide an integration of these principles into the framework of the EMC engineer.

Mr. James C. Toler, a professional engineer at the Georgia Institute of Technology Experimental Research Station, was invited to chair the session on EM Wave Interaction With Biological Systems.

EM Field Interactions

The first paper in the session was given by Dr. Q. Chen of the China Aviation Research Institute for Standardization, Beijing, China. This paper, which dealt with hazards of EM fields (both pulsed and continuous wave) and safety thresholds, suffered a great deal due to the language barrier. Chen had a lot of data which was very involved and which could not be dealt with adequately through "reading" the paper. However, some of the results that he obtained were quite interesting. His paper dealt with functional relations between EM field power density and LD_{50} and ED_{50} of animals. He has done some unique analyses of experimental data on the effects caused by the change in intensity of EM fields between 2 and 3 GHz to animals (rats). Using statistical methods, he attempted to derive a safety threshold for hazards of microwaves to humans based on what he saw for the animals. He concluded that the threshold for humans was similar to that for the rats.

In direct contrast, the next paper, given by Dr. Thomas Tenforde of Lawerence Berkeley Laboratory, was a study in clarity and didactics. His paper dealt with the effect of stationary magnetic fields on ionic conduction processes in biological systems. Based on the fact that the Lorentz force exerted on moving electrolytes (charged particles) leads to interactions between an applied stationary magnetic field and the electrical conduction processes that occur as part of several biological functions, Tenforde and his group have looked for alterations in the properties of several biological systems during the application of stationary magnetic fields up to 2 Tesla (1 Tesla = 10,000 Gauss). He reported on their experiments using sensitive electrical recording techniques to detect and measure alterations in the cardiovascular, nervous, and visual systems. All of these systems are very "electrical" in nature and depend highly

on ionic conduction mechanisms in carrying out their functions.

In order to understand Tenforde's approach, it is necessary to recall how the Lorentz force acts on moving electrolytes. The Lorentz equation simply states that the force, F, experienced by a charge, q, moving with velocity, v, is:

$$F = q[E + (v \times B)], \qquad (1)$$

where E and B are, respectively, the electric field intensity and the magnetic flux density, and $(v \times B)$ is a vector cross-product. Tenforde applied the Lorentz force law to ionic conduction processes such as the bulk flow of blood and the propagation of nerve impulses and used simple models of magnetic field interactions that could be tested experimentally. He and his group studied the magnetic field effects on ionic conduction processes in the circulatory system, on bioelectric properties of isolated neurons, and on the electrical response of retinal cells to photic stimulation. While they found some slight alterations in the electrical properties of tissues during exposure to stationary magnetic fields, these were completely reversible when the exposure was terminated.

The next paper reported on an interesting combination of therapeutic techniques: *high* pressure oxygen (HPO) and magneto stimulation. Dr. N. Dekleva, a medical specialist in general surgery from the Clinical Hospital Center of the Medical Faculty, Belgrade, Yugoslavia, spoke about the use of these two techniques in reestablishing antibiotic bactericidal action. Dekleva's hospital is near a main highway, and his team of surgeons see a lot of trauma cases which often are followed by infections caused by anaerobic bacteria. Dekleva, it seems, had a theory that bacteria which had become resistant to antibiotics might be rendered less resistant in the presence of HPO and pulsing magnetic fields.

It was not clear from Dekleva's presentation just what part he thought the magnetic fields played in altering the sensitivity of bacteria to antibodies. That the HPO should affect the action of anaerobic bacteria is rather straightforward. However, a number of clinical cases were presented in which it seemed that the combination of HPO and magnetic fields altered the course of severe infections. In several cases, bone that had resisted healing was found to heal after these therapies were applied. This is not surprising in light of the thousands of cases of the successful treatment of pseudoarthroses and other nonunions with pulsed magnetic fields.

Dr. A.J. Berteaud of the Centre National de la Recherche Scientifique Laboratory of Physics in Thiais, France, gave a paper in which he outlined some of the mechanisms of microwave power dissipation in living tissues. He presented some recent results on the variation of dielectric constant for ion free solutions and mixed ion-protein solutions. He then discussed microwave power dissipation in macromolecules with polar elements, with particular emphasis on vibrational modes, and, finally, possibilities of specific interactions with cell cytoplasm and membranes.

As Berteaud pointed out, a lot of research has been directed at various aspects of the interaction of electromagnetic fields with living tissue at different levels of organization. It has been determined that EM heating is significantly different from that caused by other modalities--for example, by infrared. Several interaction mechanisms seem to be responsible for the specificity of EM thermal conversion, and there is a characteristic dependence on frequency for different substances. The experiments conducted by Berteaud and his collaborators were designed to examine in detail some of these dependencies in several types of systems.

First, he reported on studies of the hydration of proteins and ions, done by A. Michel, F. Henry, M. deVillardi, and M. Delmotte of his laboratory. They compared two types of solutions: ionic solutions (Na, K, and Ca) in concentrations ranging from 0 to 200 mmol/L and mixed ion-protein solutions with human albumin and lysozyme as proteins. This is the first time that anyone has reported dielectric measurements on hydrated proteins and ions together in the vessel--which more nearly approximates a living tissue situation.

Berteaud also reported on studies of microwave energy absorption in macromolecules. This relates to another possible specific mechanism of absorption of microwaves due to vibrational modes within these molecules. It is postulated that any interaction that enhances the amplitude or mixing ability of the vibrational modes can change the conformation or alter the functional reactivity of the macromolecules. As is well known, Prohofsky (1975), Eyster and Prohofsky (1977), and several others have made mode calculations that show that energy absorption can take place in helical DNA by resonant interaction of the microwave field with its vibrational modes. Recently, US Office of Naval Research contractors--Dr. Chris Davis

along with a graduate student, Glenn Edwards, and Dr. Mays Swicord of the US Food and Drug Administration (see Edwards, Swicord, and Davis, 1983)--found that the microwave absorption of DNA in aqueous solution can be very large and depends on the chain length.

The final study presented by Berteaud was one actually carried out in conjunction with a group at the Pasteur Institute in Paris. I reported on this project in *ESN* 38-8:420-422 (1984) following a visit to Paris last year. In brief, the purpose of the study was to determine whether the thermal action of microwaves on cellular components is different from that due to classical heating. In order to do this, Dardalhon et al. (1984) studied changes in the microviscosity of the cell cytoplasm and in the cell membrane permeability of chinese hamster V79 cells. Changes in the microviscosity were obtained from measurements of the fluorescence depolarization of fluorescein molecules produced by enzymatic hydrolysis of the nonfluorescent substrate fluorescein diacetate (FDA) in the cytoplasm. The group also measured parameters such as cell membrane permeability, cell viability and change in FDA hydrolysis.

The paper with the most unusual visual effects was certainly that of R.G. Olsen of the Naval Aerospace Medical Research Laboratory, Pensacola, Florida. Dr. Olsen presented a lucid paper on the measurement of specific absorption rate (SAR) in a full-size man model and actually brought along one of his models, which are constructed from plastic. In his paper, he discussed an extensive study designed to measure SAR in human phantoms near a 10.67-m monopole antenna/ground plane system operating at 2.101 MHz. He has already published a paper on the use of such a model (Olsen, 1982).

Olsen told how he constructed a 68-kg model of a human by sewing together two pieces of extrusion-coated plastic material cut in the general shape of a human, and filling the resulting bag with a muscle-equivalent material. The bag material was actually a woven mat of extruded polyolefin ribbons covered on both sides with polyethylene. The model was nearly watertight and had good thermal stability. A parachute harness was used to hold the model upright. The EM-field generating system used by Olsen consisted of a 10.67-m monopole antenna (Shakespeare #666) that was mounted on the ground at the approximate center of a 30.5-m × 17.5-m wire mesh, which served to create a ground plane.

The sewn-bag human model was used over a period of 10 days in conducting the experiment and apparently held up rather well with only small signs of degradation. The internal temperature of the model was found to be very stable as long as it was shielded from direct sunlight and strong wind. Thus Olsen feels this type of model is potentially useful for obtaining SARs in the field environment. He also mentioned that the model can be used in the sitting position.

The final paper in this session also dealt with a model of a human. This paper, given by Professor D.W. Griffin of the Department of Electrical and Electronic Engineering, the University of Adelaide, Australia, dealt with an image-plane type model of a human head. The objective of the study, as reported by Griffin, was to determine the scattering effects of metal-framed safety glasses on microwave fields impinging on the head in the region of the eyes.

With as much interest as there has been on microwave cataractogenesis, it is quite surprising how little thought has gone into the possible perturbation of the field by such things as metal-framed safety glasses. As Cleary (1980) pointed out, the true measure of the cataractogenesis hazard is the energy absorbed directly by the eye. Yet, while microwave cataractogenesis is one of the most extensively studied exposure effects the influence of such variables as frequency, field polarization and directions of incidence on the distribution of microwave energy near and in the human eye has received little attention.

Griffin and his coworker, Dr. N. Davias, suspected there might be significant scattering of incident microwave energy because the metal frames of safety glasses include closed loop sections extending to the ears. They thus developed a very sophisticated system for determining the effect of such glasses and tested it at 2 to 4 GHz (Griffin and Davias, 1984). In this paper Griffin spoke of the extension of this study to 12-GHz microwaves.

It was clear that for measurements with a monopole antenna that extends past the pupil of the eye, introduction of metal-framed glasses causes an increase in the intensity by up to 5 dB for one field polarization and up to 20 dB for another. This was true for a wide range of frequencies and orientations. Griffin's data clearly indicated a need to give more attention to the matter of glasses and goggles when considering the exposure of human eyes to a microwave field.

Conclusion

Following the presentation of the papers, the chair, Mr. Toler, summarized the high points and pledged to involve the EMC community more in the area of biological compatibility through future sessions such as this one.

For more details about the conference, see ONR, London, conference report C-3-85, which you can order by using the mailer inside the back cover of this issue.

References

Cleary, S.F., "Microwave Cataractogenesis," *Proceedings of the IEEE*, 68 (January 1980), 49.

Dardalhon, M., C. More, D. Averbeck, and A.J. Berteaud, "Thermal Action of 2.45 GHz Microwaves on the Cytoplasm of Chinese Hamster Cells," *Bioelectromagnetics*, 5 (1984), 247.

Edwards, G.S., M.L. Swicord, and C.C. Davis, "Microwave Absorption Characteristics of Highly Purified *E. coli* DNA," paper presented at the Fifth Annual Meeting of The Bioelectromagnetics Society, Boulder, Colorado, June 1983.

Eyster, J.M., and E.W. Prohofsky, "B to A Confirmation Change of Double Helix," *Biopolymers*, 16 (1977), 965.

Griffin, D.W. and N. Davias, "The Effect of Metal-framed Spectacles on Microwave Radiation Hazard Near the Eyes," paper presented at IEEE 1984 National Symposium on Electromagnetic Compatability.

Olsen, R.G., "Far Field Dosimetric Measurements in a Full-sized Man Model at 2.0 GHz," *Bioelectromagnetics*, Vol 3, No. 4 (1982), 433.

Prohofsky, E.W., "Predictions of Giant Breathing and Rocking Modes in Double Helical RNA," *Physics Letters*, 50A (1975), 329.

4/22/85

Chemistry

CHEMISTRY IN EUROPE: AN OVERVIEW

by David L. Venesky. Dr. Venesky is the Liaison Scientist for Chemistry in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on reassignment until October 1986 from the Naval Research Laboratory, Washington, DC, where he was the Head of the Inorganic and Electrochemistry Branch and Associate Superintendent of the Chemistry Division.

In the past 6 months, I have visited 14 universities in nine European countries and have interviewed over 100 chemists. Some of the discussions about mutual research interests strayed from technology to some of the common problems in any research department: not enough funds, students or technicians not as good as years before, insufficient state-of-the-art equipment, and too much administrative work. These common factors, along with other general observations, contributed significantly to my understanding and appreciating the type of chemical research being done at a specific institution. Before going into depth in later articles about individual departments or individual chemical research groups, I believe a few preliminary general remarks will allow the reader to better appreciate the chemical research in Europe.

My remarks will be limited to work from Trondheim, Norway, in the north to Granada, Spain, in the south and from Reading, UK, in the west to Strasbourg, France, in the east. Noticeably absent from this article are the chemical departments in West Germany, Israel, Austria, Italy, and several countries having minor impact on the field of chemistry. In addition, I have made only a minimal number of visits to the highly important and active groups in the UK in order to have adequate time for the Continent.

The focus in this introduction will be on the basic chemical research in England, France, Belgium, The Netherlands, Denmark, Sweden, Norway, and Spain. Thus, the discussion will include chemistry not only in highly industrialized countries competing in worldwide trade like France, the UK, and The Netherlands, but also in Spain, a country with a fraction of the internal industrial resources as the others and only concerned with its internal trade. The differences in educational systems and areas of chemical research were surprisingly closely coupled to the industrial outlook of the country visited. Although political problems are definitely important, no mention of these will be made.

Employment Opportunities for Chemists

The relationship between the employment of chemists and the industrial health of a country was evident. In The Netherlands, Belgium, and Denmark, where

industrial expansion is continuing, the supply of chemists having the equivalent to the bachelor's degree in the US is far less than the demand. France, the UK, Sweden, and Norway are experiencing a leveling of industrial expansion and reported no serious shortages of chemists. Chemists at all levels of education exceed the demand in Spain, where industrial expansion is still to come.

In several countries the word *chemistry* has such a negative connotation (because of such nationally publicized terms as Bhopal, North Sea pollution, synthetic hallucinatory drugs, carcinogenic chemical wastes, and undetected organic vapors) that students do not want to enter the profession. Public relations is sorely needed to emphasize the good that chemistry plays in our world today. The American Chemical Society and its committees on public relations and international affairs should investigate means to assist in changing the attitude toward chemistry in Europe. Interestingly, at Aarhus University, Denmark, the Chemistry Institute is attempting to attract more students into chemistry by planning combined degrees in chemistry such as chemistry/biotechnology and chemistry/computer sciences.

According to several chemistry professors, the top UK university students graduating with first level degrees in chemistry, are changing fields, and a surprisingly large number of graduates are entering accounting and banking firms. Those UK students having the poorest grades go to laboratories as technicians, while the remaining average and above-average students go on to graduate studies. Of course, these observations are trends and may vary according to university.

One important factor in job hunting in Europe is the strong personal desire to remain close to one's birthplace--a situation true in the US 30 or 40 years ago. Thus in Spain you find secondary school teachers with the equivalent of PhD degrees in the location of their choice, rather than in a more industrial region such as Barcelona, Madrid, or even another country in Europe with better positions. I doubt that this situation will change even if Spain enters the European Economic Community (EEC).

The Student of Chemistry

The source of chemists naturally begins with a student selecting a college. Again the situation differs depending on the country. For example, in the UK the number of entering students is limited by law. The larger universities, such as Southampton and Leeds, have a limit of 80 or 90 students entering the chemistry curriculum. I was amazed to find how these students are selected from an original number of nearly 300 or 400 applications. Up to 200 may be selected to visit an institution to meet the faculty and review the facilities. After such a visit, a university committee must make the final selection. At Southampton I was told all of the 200 or so applications are reviewed and individually answered--probably thanks to computers!

In other countries the number of students admitted to chemistry programs also is restricted, but the quota is seldom filled. Most of the universities I visited had in their graduate programs foreign nationals who were supported by their home governments. Although most faculty members said they could use more assistance in their research, most were satisfied with the number of students available. Most considered their students highly qualified and well above average.

A new program at the University Louis Pasteur, Strasbourg, France, is the Trilingual European Program in chemistry, which started 3 years ago and includes instruction in French, German, and English. The chemical engineering students will have their courses taught by visiting instructors in one of the three languages. So far, students from France, the UK, and Germany are participating. Later, Norway will participate if financial help from the EEC and industrial companies is available to the program. Students from England (Leeds, Surrey, Guildford) and Scotland (Stirling) are participating.

A review of chemistry programs is beyond the scope of this introduction, but I will try in future articles to identify unusual educational programs or courses of instruction; because I am focusing on research and not education, I will emphasize the former and not the latter. Of course, most important to research and education are the faculty and department resources.

Faculty and Resources

Any attempt to compare the quality of faculty from one university to another is impossible. Again, only general impressions can be given. Visits to universities where so many famous chemists and other scientists worked make one realize the greatness of many of the universities in Europe. In the coming months, I will detail the work at the various institutions and specifically highlight the current, most promising new areas of research. Although I started with the hope of reviewing only

limited areas of chemistry, I found myself spreading to as many areas as possible within the limited time of my visits.

All countries I visited have a single governmental organization that directs the funds for faculty research and teaching. The complexity of the organization varies. For example, the Centre National de la Recherche Scientifique (CNRS) in France operates through a committee of peers, CNRS laboratories, associated university laboratories, and CNRS researchers in university laboratories (see page 341). Several observations: once established, associated laboratories are never dissolved; there are conflicts between the CNRS employees (union members) who do only research and the teaching faculty of the same rank doing research and teaching; and the favoritism shown by a committee of peers is not without politics. When there is a good balance in research funds available, the disadvantages of the directed research are minimized. For example, at the University Louis Pasteur in Strasbourg, the sources of funding for chemical research is almost equally divided among CNRS, private or industrial funding, and the ministry of education funding. A highly productive research center has evolved with excellent cooperation and interaction between groups of researchers (see next article).

Other countries control research and teaching funds in a less complex fashion, but all show some distinctive feature on how the funds are governed. In The Netherlands, a committee of 32--consisting of faculty, students, and technicians and support-staff--has a major role in approving the use of funds for chemical research. Although the committee is showing less control over scientific research, it does exist and could readily direct funds away from a science with a bad name, such as chemistry is believed to have.

In Spain, the Consejo Superior de Investigaciones Cientificas (CSIC) is the group that controls CSIC laboratories and institutes, and university funds for research (*ESN* 38-6:336-338 [1984]). The political nature of the *consejo* is noted by the excellent array of instruments at some universities and the unusual lack of common instruments such as nuclear magnetic resonance and mass spectrometers at other departments. In Spain the CSIC has emerged as a powerful unit directing chemical research so that industrial products and new industry will emerge. Unfortunately, the research so far reviewed reveals a long and hard struggle to attain that goal.

In general, the research I have reviewed in the European countries I visited revealed specific centers of excellence. For example, the universities in Sweden (Goteborg, Stockholm, and Uppsala) have the highest concentration of x-ray, neutron, and other spectroscopies for characterizing and determining the structure materials. In Norway (Oslo and Trondheim) the emphasis is on electron diffraction in the gas phase. Consequently, you have to put Scandinavia at the top of your list if you seek assistance or collaboration in structure analysis.

Catalysis is one of the main emphases of research in countries heavily involved in petroleum and petroleum products. Consequently, in both Norway and Holland there is strong emphasis on the synthesis of catalysts, the understanding of the catalytic process, and the determination of ways to influence the end product. In France, the University Louis Pasteur and the many CNRS institutes and associated laboratories in Strasbourg have the most extensive effort in the field of catalysis; from simple thermodynamic studies to synthetic and kinetic studies of a host of inorganic catalytic systems (see next article). As I traveled throughout Europe, I found most collaboration on catalysts and related topics was between chemists at Strasbourg and other chemistry departments in France and other countries.

Another example of a center of excellence in a specific area is Southampton, UK. Because electrochemistry is an area I will be reviewing in more detail than others, I made my first visit in Europe to the University of Southampton. There the group of 15 or so principal investigators represents the world's highest concentration of experts in electrochemistry. Wherever electrochemistry is being investigated, collaboration with Southampton is evident, or a faculty member, student, or postdoctoral fellow has spent time or graduated from the UK department. I'll provide a detailed look at this research group in a later *ESN*.

As stated earlier, I have only covered a fraction of the chemistry departments and a limited number of researchers in my initial visits, so there are certainly gaps and oversimplifications in these first impressions.

In general, I found most chemistry faculty members had at some time in their careers spent time in the US on sabbaticals or as postdoctoral fellows. Many European faculty members have collaborated or are now collaborating on

research projects with chemists in the US. This close interaction between the chemists in Europe and those in the US was greater than I expected.

Future Articles

This introduction gives my first impressions of the chemistry departments in the countries visited. This was not meant to be a comprehensive report, but a review to set the stage for more detailed articles about the chemistry in Europe and the Middle East. In future articles, I will emphasize specific research groups and their investigations. Where a study is being conducted that I believe could affect current chemical research, I will report these as a *Science Newsbrief* in a more timely fashion than the *ESN* articles. For the US chemists coming to Europe, I am available to assist in providing contacts or arranging visits.

4/19/85

OVERVIEW OF STRASBOURG, THE CENTER OF CHEMICAL RESEARCH IN FRANCE

by David L. Venezky.

My first visit to a chemistry department on the Continent was to the University Louis Pasteur (UPL) in Strasbourg, France. I was aware of the high level of chemical research at the University, but I was unaware of the complexity of the organization and the extent of participation by the Centre National de la Recherche Scientific (CNRS) in the funding and directing of chemical research at the institution (see page 341). Before reviewing in future *ESN*s individual research groups, I believe a general review of the university's history and the organization of the various research groups at Strasbourg would help the reader appreciate the broad scope of chemical research in this interesting city.

Strasbourg began its history as a university center in 1567, when the first academy was established. Soon after Emperor Ferdinand II converted the academy into a university (1621) with four faculties, its academic work became known throughout Europe.

Over the centuries the university grew in stature to its present organization as a powerful scientific center. University I or "Louis Pasteur," the "scientific" organization, has interwoven into its academic structure research groups belonging to the CNRS and the Institut National de la Santé et de la Recherche Medicale (INSERM). The former organization is the most important contributor to the funding and direction of chemical research in France.

In addition to University I, the scientific organization, Universities II and III--which are devoted to arts, social sciences, and law--complete the combination of subjects in science, medicine, and the humanities that makes Strasbourg a truly and outstanding academic center of knowledge in France.

The University Louis Pasteur (ULP) is divided into 15 "teaching and research units" involving faculties (medical and biomedical sciences, odontology, pharmaceutical sciences, physics and chemistry, mathematics, matter sciences, life and earth sciences, behavioral sciences, economy, geography, astronomy, geophysics) and engineering schools (chemistry, geophysics, physics, polymers). Over 1300 faculty members teach roughly 13,000 students; about one-fourth of the students are engaged in research. In chemistry, as in other fields of research, the faculty members teaching and working for or associated with CNRS become difficult to ascertain. No wonder the *Chemical Research Faculties, An International Directory (1984)*, published by the American Chemical Society, lists a "Department of Chemistry" and several institutes, and makes the statement: "All faculty members are listed following the Centre de Recherches sur les Macromolecules." Even after a week and many attempts to understand the complex organization, I admitted defeat. For such a seemingly disorganized group of chemists, the organization promotes much interaction, collaboration, and cooperation.

In chemistry, about one-third of the research funding originates from the CNRS. Consequently, a large effort goes to protecting funds, requesting new funds, or suggesting consolidation of existing research. The CNRS influence on chemical research is always evident. During my visit in January, all of the principal investigators were preparing their CNRS progress reports for 20 January.

Strasbourg is the second largest CNRS research community in France, with funding principally directed toward nuclear physics (38 percent), biology (29 percent), and chemistry (14 percent). Over 500 scientists and 1000 engineers and technicians are employed in Strasbourg by CNRS and INSERM. Most of these employees work in the

12 CNRS-owned laboratories, or in more than 50 university laboratories that are "associated" with CNRS by virtue of a CNRS-directed research thrust.

For example, the "Unité Associée No. 405, Physico-chimie de la complex et des system interfaces" is a CNRS research thrust that brought together over 60 researchers under the direction of Professor Maurice Gross. Gross heads the Laboratoire d'Electrochimie et de Chimie-Physique du Corps Solide in the Institut Le Bel, which is a part of the ULP, and includes other principal investigators in the associated unit in the area of electrochemistry. To add more confusion to my understanding the organization of the CNRS associated unit, the term "school of engineering" within the university connotes a much different course of study and research than in the US. Thus, the principal researchers from the school of engineering, École Nationale Supérieure de Chimie de Strasbourg, also in the unit are Professors Marie-Jose Schwing, Jean-Louis Leibenguth, Jean-Paul Schwing, and Maurice Leroy.

Included in the associated unit of 90 to 100 researchers are graduate students, technicians, and CNRS employees. Although harmony among the faculty and CNRS employees is apparent, several university professors confessed a jealousy between the members of the university faculty required to teach and do research and the CNRS employees required only to do research. However, most CNRS researchers I met did have graduate students working for them and occasionally taught courses. When a CNRS employee, who is a union member, is promoted to "Director of Research," that is equivalent to a full university professor in all senses of the word. I heard comments that the teaching staff did not approve of this high rank for one who had less teaching responsibility and academic standing than they. Other CNRS ranks are "Charge de Recherches" and "Maitre de Recherche"--equivalent to assistant and associate professors on the US scale, respectively.

The broad areas of research covered in Unité Associée No. 405 are thermodynamics, kinetics, extraction and phase transformation, fundamental and applied electrochemistry, macrocyclic chelates, metal clusters, and spectroscopic properties of complexes in solution. My impression after discussing the research of most of the principal investigators of this unit is that their research has changed little from what was being done before the consolidation. If anything, the reorganization had little effect on the research. The funding within the unit remained the same: equal portions from the Education Ministry, CNRS, and industry/private sector. Because of the extensive cooperation and collaboration in the ULP, I am uncertain if it increased with the formation of the associated unit.

A more detailed review of the research of the individual investigators will be the subject of future articles. However, I would like to complete this article by listing other "laboratories" or, in a sense, the title of the chemical research groups headed by principal investigators within ULP. Some of the principal personnel have been mentioned above, but are again listed for clarity.

Institute Le Bel

1. Laboratoire de Chimie Organique Physique. Professor Jean-Marie Lehn. Best summary of the excellent work from this group is presented in "Supra-Molecular Chemistry: Receptors, Catalysts and Carriers," *Science*, 227 (1985), 849-856.

2. Laboratoire de Cristallochimie et de Chimie Structure. Professor Raymond Weiss. Synthesis and study of enzymatic sites in metallo enzymes and macrocyclic complexes and porphyrins. New sandwich materials for electrochromics and semiconductors.

3. Laboratoire d'Electrochimie et de Chimie-Physique du Corps Solide. Professor Maurice Gross, Paul Lemoine, A. Giraudeau, and Pierre Chartier. Mechanism of reactions between electroactive species at electrodes, including electrontransfer in metallo-organic compounds such as cryptates and porphyrins, macrocyclic chelates, and clusters. Electrochemistry and photoelectrochemistry applied to energy conversion.

4. Laboratoire de Chimie Inorganique Moleculaire et de Catalyse. Professor John A. Osborn. Macrocycles, copper complexes, and organo-metallics as catalysts. Kinetics and mechanisms of catalytic processes giving specific products and structures.

5. Laboratoire de Catalyse et Chimie des Surfaces. Dr. Gilbert L. Maire, Maitre de Recherche, CNRS, Hydrodenitrogenation mechanisms on catalysts, skeletal rearrangement of hydrocarbons on metal and oxide catalysts by studying surface chemistry.

6. Laboratoire de Chimie de Coordination. Dr. Pierre Braunstein, Maitre de Recherch, CNRS. Transition metal clusters, carbonyl and phosphorus containing ligand complexes used in the investigation of carbon monoxide and carbon dioxide activation.

Institute de Chimie

1. Laboratoire de Chimie Organo-Minerale. Professor Jean-Pierre Sauvage.

Synthesis of chelating ligands and their complexes for specific fixation of small substrates (O_2, N_2, CO, CO_2). Activation of small molecules through coordination compounds.

2. Laboratoire de Chimie des Porphyrines. Dr. Henry J. Callot (CNRS, Maitre de Recherche). The chemistry of porphyrins, including electrochemical and catalytic properties.

3. Laboratoire de Chimie Organique Appliquée. Professor Alain Kiennemann. Mechanisms of heterogeneous and homogeneous catalysis in carbon oxide-hydrogen reactions to produce alcohols and hydrocarbons.

4. Laboratoire de Geochimie. Dr. Pierre Albrecht, Directeur de Recherche, CNRS. Molecular organic geochemistry of sediments and petroleums. Fingerprinting of microorganisms is applied to explorations and coal reforming, through analytical approach to natural products and precise structure elucidation.

École Nationale Supérieure de Chimie de Strasbourg

1. Laboratoire de Chimie-Physique. Professor Marie-Jose Schwing. Thermodynamics of complexes formed between transition metals and lanthanides and macrocyclic ligands. Stabilization of unstable oxidation states.

2. Laboratoire de Chimie-Physique et Electrochimie. Professor Jean-Paul Schwing. Kinetics of complex formation and stability of macrocylic compounds and carboxylic ionophores by stopped-flow and T-jump techniques.

3. Laboratoire de Chimie Minerale. Professor Maurice Leroy. Liquid-liquid extractions, liquid membranes, application to trace metal analysis.

Centre de Recherches sur les Macromolecules

Professor Gilbert E. Weill and Bernard Francois, Maitre de Recherche, CNRS, are the principal investigators at this center. Within the center there are divisions investigating basic polymer science to characterize and determine the physical properties of polymeric materials, colloids, emulsions, liquid crystals and conducting polymers. Rheology of polymers in the condensed state is investigated by neutron scattering and deuterating co-polymers, blends, and interpenetrating polymers. Also investigated are physical aging of materials, crazing, and understanding epitaxial growth on surfaces of semicrystalline polymers.

Conclusion

The complex structure of the chemical research organization at the University Louis Pasteur is difficult to understand if not impossible to decipher. Regardless, the productive chemical research at Strasbourg is outstanding and the reason the city is considered one of Europe's strongest centers of chemical research.

4/19/85

Computer Sciences

EXPERT SYSTEMS AT BARCELONA

by P. Roman. Dr. Roman is the Liaison Scientist for Physics in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on assignment until September 1987.

Artificial intelligence (AI), a somewhat unfelicitous catchword, comprises many things and, after a false start in the 1960s, is now likely to become a multi-billion dollar business by the 1990s. It is hard to define the field, but probably it is correct to say that AI is a science focused on developing generalized conceptual, computational, and symbolic approaches to intelligent behavior.

All areas of AI work have both industrial and often very high military significance. The major AI activities cover robotics, natural language and speech understanding, speech synthesis, automatic translation, automatic programming, computer vision, smart computer-aided design and manufacturing, symbolic mathematical problem-solving, and foremost of all, expert systems (ES).

ESN has carried several reports on AI topics, including ES. They were written with the knowledge and from the viewpoint of computer scientists. I, however, am a physicist and focus on other, more mathematical and theoretical aspects of AI topics. (Examples of my approach can be found in *ESN* 39-5:190-192 and 39-6:250-252 [1985].) In this article I report on certain aspects of ES research I observed during a trip to Barcelona, because I believe that the selected topics or approaches I have chosen are not only of high quality but actually are closely related to certain key points of concern of ES work by the US Navy. Specifically, they are relevant

for solving difficulties with the speed with which knowledge in the building of an ES system is acquired, with the role of inductive inference as well as "common sense" procedures in the context of automated reasoning, and with two areas of knowledge representation--namely, the coordination of multiple representation schemes and the representation of "plans."

The original and narrow definition of an ES is that its purpose is to emulate the performance of a human expert at a high level (or better still that it is a set of computer programs and manipulations which resemble human expert evaluation, problem resolution, and decision making by applying the technique of logical inference). But in actual fact, ES techniques and concepts are the very basis of all AI applications. After all, an ES contains a knowledge base (consisting, usually, both of facts and rules, and also of heuristics), a logical inference machine, and a track-keeping current data base; an ES has also input-output interfaces, that often themselves are "experts" in communicating with humans, instruments, and peripherals. In turn, all these components and functions are, of course, various aspects of AI. The immense potential of ES for, say, naval applications can be illustrated in one example. A naval task force explores by means of a variety of sensors--such as satellite surveying, active and passive radar, microwaves, infrared, thermal imaging, and sonar, all operating from different platforms and at different locations--a large number of very different kinds of information about a distant area of the ocean. An ES, properly interfaced with signal processing units (which themselves may contain ES components), evaluates, with its "expertise" and constantly adjusted knowledge base, the information and makes a diagnosis of what "naval objects" are out there in the distance, explaining also to the human operator how the conclusion has been reached and what likelihood of errors or misinterpretations are to be reckoned with. But this is when the real job of the commander begins: What actions, if any, should be taken? What alternatives are there and what risks? Another ES (linked to the first) should use the combined knowledge, experience, judgment, and logic of many naval officers to answer these questions--and in real time, too!

For some reason (could it be genetic?) Catalonia always has been a European leader in computer science and related areas. Out of the many centers in and around Barcelona, I have selected three: the Facultat d'Informatica of the Universitat Politècnica de Catalunya, the Instituto de Cibernética, and the Departamento de Informática at the Universidad Autónoma de Barcelona. (For a general review of scientific research in Spain, see page 333.)

Learning Systems for "Soft" Knowledge Areas

Professor R. López de Màntaras at the Faculty of Information Science of the Polytechnic University is primarily concerned with the task of teaching expert systems solid knowledge in areas where facts are not always quantifiable.

He pointed out to me that learning is not a mere accumulation of *data*; it is better to regard it as accumulation of *information*. The meaning of information, in this context, is that it embodies some structural properties defined on the set of data. Now, accumulation of data leads to saturation, but accumulation of information also has its dangers: it may lead to overwhelming complexity. Thus, it is necessary to introduce a "forgetting mechanism" in such a way that relevant characteristics of the set of data are kept, whereas descriptions of individual data are lost. Consequently, the initial set will appear as a set of clusters of similarity classes, and only the parameters that are necessary to define these classes or subsets are to be stored. Going further one essential step, in order to follow the natural procedures of learning and perception it seems natural to replace equivalences by similarities and therefore "hard" concepts by "soft" ones. When doing this, the result of a learning procedure for data classification becomes a "fuzzy partition" of the set from which the observed data are drawn.

This is not the proper place to elaborate on the exciting modern mathematics of fuzzy sets and fuzzy logic. Suffice it to say that this discipline is based on the need to deal with uncertainty and imprecision. These are different concepts. Indeed, a proposition that makes a statement about the value of some variable is imprecise if such a value is not sufficiently determined; but a proposition is uncertain if its truth cannot be clearly established. Therefore, a proposition can be precise but uncertain, and another proposition may be certain but imprecise. A calculus of possibility, credibility, and plausibility can be developed in a systematic manner within the framework of fuzzy sets and logic. López de Màntaras suggests that, irrespective of the special nature of the domain, fuzzy logic provides a natural framework for knowledge

representation (through a tool called possibility distributions) and also for inference from knowledge bases that are imprecise, incomplete, or not totally reliable.

While, apart from emphasis on generality, this viewpoint of López de Màntaras is surely not unique among AI experts, he went a long way in making it a practical tool for the classification and linguistic characterization of nondeterministic data. Continuing his line of argument about the learning process we surveyed above, he explained that after an initial learning period the system must fulfill two functions: (1) modification of previous memory (or estimation), and (2) modification of the confidence (or belief) in this previous memory. In his high level work, he then took this unavoidable sequential classification as a problem of estimation of a fuzzy partition. He showed that parameters of membership functions can be estimated recursively by a learning or self-learning mechanism. Furthermore, he succeeded in describing classes by multivariate possibility distributions. He showed that the marginal possibility distribution for one of the components describing an object can be matched to a possibility defined on the interval [0,1], chosen among a set corresponding to linguistic labels such as "low," "high," "very high," "extreme," and a label can be associated with this component. He then intimated that a higher level learning may be introduced to modify the semantics of the linguistic labels.

This research, recently concluded, was done in cooperation with Dr. J.A. Martin in Toulouse, France, and was supported by the Spanish-French scientific cooperation program. Present efforts of López de Màntaras (in association with Dr. C. Freksa, Munich), made possible by a grant from the Catalonian regional government, focus on implementing a higher level of learning in order to establish a dialogue between the learning system and an external teacher, with the goal of adjusting or updating the semantics of the linguistic labels. His current work focuses on a human-guided feature-classification system. By reference to examples, a person teaches the "meaning in context" of subjective feature descriptors to the computer system. The resulting knowledge base of the system is then used in a classification phase for the interpretation of descriptions made by the teacher. These descriptions are communicated by semantic translations of subjective descriptions. López de Màntaras is convinced that this subjective linguistic description scheme has a great advantage over more traditional schemes, because it possesses high descriptor-feature consistency. Moreover, by this approach a high feature resolution for the overall cognitive perception and the description process is achieved. He summarizes his entire effort by saying that he can now build an expert system for pattern description which combines expertise of a human observer with memory, combinatoric ability, and high speed.

Since López de Màntaras' results demonstrated that "soft," incomplete information can lead to an admittedly imprecise and fuzzy image that, despite its coarseness, is nevertheless a correct representation of a given situation, and since his current endeavors are particularly suitable for domains in which "expertise" has not yet been properly formalized, his research deserves serious attention from the US Navy AI community. Perhaps it may be worthwhile to also mention that López de Màntaras is Spain's designated External Observer to the European Economic Community's cooperative project in computer science, ESPRIT.

More Intelligence for Robots

Improving methods for three-dimensional "vision" and better "conversation" with robots are, for me, the most interesting areas of research at the Cybernetic Institute. But I will first generally describe this institute because it is bound to play a strong role in the future of AI work in Spain.

The institute originated as a section of the Catalonian Polytechnic University's computer science department, but in 1975 it was joined to units of the government research council (CSIC; see the article on page 333). Ever since, under the title of Instituto de Cibernética, it has enjoyed a well-balanced budget and has had a strong and developing structure and a good reputation. The director, Professor G. Ferraté, is chiefly responsible for the large-scale instructional activities, and the vice-director, Dr. L. Basañez handles research with much skill. There are 30 PhD researchers and about 14 students in the institute, and visiting scientists are always around. The strength of the infrastructure of the institute is well demonstrated by the fact that, apart from having preferential access to the polytechnic's mainframe central computer, they also have a dedicated VAX785, a modern EAI hybrid digital-analog computer with two development stations (Intel and Tectronix),

and a Puma robot. Much of their relative prosperity stems from having good industrial relations. (Examples of their work with industry include a contract with the Electric Company for devising control systems, projects on civilian naval automatic guidance systems and port traffic control, and simulation work done for the machine industry, hydrology, and the social security service.) They also have had past grants with the US National Science Foundation and selected US universities.

Now, the specific topics I want to describe briefly are done in the Artificial Intelligence and Robotics work group and aim at efficiently solving basic problems of robotics by using fundamental expert system and knowledge-based logic methodology.

Professor A. Sanfeliu is improving innovatively the three-dimensional (3D) vision capabilities of AI systems. In his latest work he treats the problem of recognizing 3D objects which are partially hidden and deformed by a method which uses a distance measure, based on novel tree-graph grammars. The focus of the work is on the representation and recognition process, and it is assumed that the range data, boundaries, and other features have already been extracted. Sanfeliu succeeded in representing a 3D object by a hierarchical model which is based on an attributed tree-graph grammar. (The tree-graph grammars for pattern recognition were constructed by Sanfeliu and Dr. K.S. Fu; this highly acclaimed method was published by Springer in its Lecture Notes in Computer Science series, 1982.) To approach the highly sophisticated case of 3D problems, Sanfeliu first tested his approach by examining the problems of occultation and deformation on 2D objects and studying both general considerations as well as ambiguities. These preliminary studies allowed him to develop in full a method to recognize 3D objects, where the use of a distance measure based on tree-graph grammars is combined with the use of error transformations to compute the measure.

It is interesting to compare Sanfeliu's approach to previous studies in the field. Recognition of objects is customarily based on matching a part of the scene to a part of an object model. Standard approaches use a control strategy for matching and try to reduce the number of trials by means of "useful" scene features. Clearly, Sanfeliu's hierarchical representation is a more profound start, and the replacement of matching attempts by first transforming the scene into a graph and then applying a well-defined distance measure between the scene and the troject model is obviously a more scientific, or shall we say "intelligent," approach.

Sanfeliu summarized the merits of his novel approach as follows:

1. The method does not depend on particular objects, and the classifiers are independent of the domain database.
2. Common-sense arguments have been incorporated (via the use of error transformations).
3. Already the bottom level of the hierarchy allows the estimation of the cost of recognition.

A second, somewhat unconventional effort in the same research group is being pursued by Professor R. Huber. He is specializing in intelligent robot languages. Whereas many radically different approaches have been tried since the mid-1970s to get more and more intelligent robots through specialized languages, progress cannot be said to be satisfactory. Apparently, all robot control languages are presently on the robot level and specific to the particular robot. Huber advocates a basically new approach, namely the construction of a new, high-level, universal, task-oriented language. Such a language must be developed by an expert system which is now under construction in Huber's research group. (Incidentally, he does not believe that a user-friendly robot interface taking a natural language and transforming it to the specific robot language is a workable approach.) The ambitious Huber plan implies that once a universal task-oriented robot language is available, it will be first used, as an intermediate stage, at the robot level and then only translated into any specific robot language used by the machine.

In summary, the two examples I sketched are only indicative of the vigorous and many-faceted work of the Cybernetic Institute, and surely mutual beneficial US-Spanish interactions can and should be built up in the near future.

Practical ES Efforts

My review would not be fair without brief indication of a variety of research projects carried out at the Department of Informatics at the Bellaterra campus of Barcelona's new Autónoma University. Let me preface the list by pointing out that this is also a well-equipped, past critical-size institute, under the directorship of Professor J. Aguiló Llobet; apart from the AI unit it also has an applied mathematics unit

(coding, cryptography) and an internationally recognized unit focusing on computer-aided design of integrated circuits.

The AI group is small, Professors J. Augusti and P. Villanueva being the only doctorate holders; they are assisted by about four research assistants and students. Some of their work is commissioned by the International System of Standards and develops general graphics standards. Connected with this work is a substantial effort in image processing. The researchers are trying to develop nonspecific, general software in this area, but curiously enough they finance this work by contracting with industrial outfits to work out low-level specific software for them. Their research is facilitated by a brand new VICOM system, which, despite its very high price, was purchased from straight university funds and is the second "pilot system" of this nature in Spain. (The first is at the CSIC Optics Institute in Madrid.) The image-processing work is also funded in part by the Spanish defense ministry, employing this approach to TV-tracking of aeroplanes.

Other AI work, closer to the ES area, includes work on a medical diagnosis system (claimed to be superior to MYCIN); game theory automation (again, the researchers developed, for example, an expert machine for Mastermind, proudly pointing out its increased speed as well as higher efficiency compared to the US version); and ES systems to run educational computers for children, where the AI interface allows the user to operate the sophisticated machine with no more knowledge than an acquaintance with LOGO.

Because of various constraints, I was not able to ascertain whether something really unusual is happening in the AI group of the Autónoma. Nevertheless, I am sure that this is a serious institute with devoted researchers.

Concluding Apologies

Partly because my lack of deeper training in AI, partly because of the difficulties in technical arrangements, and partly perhaps also because of some communication problems, I may not have given a fair or truly exhaustive picture of ES-related work in this article. But even from what I saw and could judge, I came to the conclusion that here we have several successful groups of scientists in an area that keeps growing in importance at a steady rate and which deserves serious attention and assistance from the US side of the Atlantic.

2/20/85

Material Sciences

SWEDISH INSTITUTE FOR METALS RESEARCH

by Kenneth D. Challenger. Dr. Challenger is the Liaison Scientist for Materials Science in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on leave until May 1986 from the Naval Postgraduate School, where he is Associate Professor of Materials Science.

Sweden is recognized as one of the world's leaders in the production of high-quality steel. Since its founding in 1921, the Swedish Institute for Metals Research (IM), Stockholm, has provided excellent research and development support for not only all of Sweden's but also all of Scandinavia's steel industries. It also receives support from some of the nonferrous metals industries from all over Scandinavia--i.e., the copper, zinc, lead, and aluminium industries. The general research program is financed by an agreement between industry (via the Swedish Iron and Metals Research Foundation) and the government (via the Swedish Board for Technical Development). About SKr13 million ($1.3 million) is spent in this general research and another SKr9 million of research is funded through contract research.

IM employs about 77 people, of whom about 54 are researchers. The main theme of research is the relationship between microstructure, chemistry and processing and the properties of metallic materials. About 80 percent of the research is on steel alloys, and the remaining 20 percent is devoted to nonferrous metals. The institute is directed by Professor Rune Lagneborg, my host.

The metals research is divided among four departments: Mechanical Metallurgy, Analytical Chemistry, Structural Metallurgy, and Casting and Powder Metallurgy.

Mechanical Metallurgy

Dr. W. Roberts heads the Mechanical Metallurgy Department. Research is performed on three general topics: (1) steels for machine parts and tools; (2) properties of stainless steels; and (3) properties of construction steels.

Steels for Machine Parts and Tools. The mechanical properties of these steels in the as-processed state are of prime importance as the research at IM

is focused on reducing processing costs by eliminating the heat treatment step of the processing. Thus, the evolution of microstructure during the various processing steps is studied. Microanalytical electron microscopy is used to study carbide precipitation in secondary-hardening steels such as high-speed steels and hot-work tool steels.

Stainless Steels. Sweden was one of the first steel makers to introduce the duplex (ferritic-austenite) stainless steels. These steels combined with other grades of stainless steel represent a substantial export market for the Swedish steel industry (over 320 kt last year). In general, the weakest point of stainless steel construction is the welds. Either the weld metal or the heat affected zone (HAZ) will have mechanical properties and corrosion resistance that is inferior to the nonwelded material. These changes usually can be correlated with local changes in the microstructure. Segregation, the formation of unwanted precipitates, and changes in the types and distribution of nonmetallic inclusions occur in either the weld metal or the HAZ as a result of the thermal cycle which occurs during welding. A nitrogen-bearing duplex steel (0.015C, 22Cr, 5Ni, 3Mo, 0.3N, bal.Fe) has been developed which has better strength and resistance to stress corrosion cracking than the fully austenistic stainless steels. One problem with the duplex stainless steels is the formation of a ferritic HAZ which can cause brittleness. The nitrogen addition assists in the reformation of austenite in the HAZ, reducing this problem.

Boron additions are known to improve hot workability, but can cause hot cracking during welding and increase the susceptibility to intergranular corrosion due to the formation of M_2B grain boundary precipitates. Research at IM has shown that for type 316L stainless steel (one of the most widely used austenitic stainless steels), 20 to 30 ppm boron can be added without adversely affecting hot cracking or intergranular corrosion resistance. However, in low-carbon 18Cr-8Ni grades such as type 304L, even small amounts of boron (5 to 15 ppm) will give rise to a very rapid M_2B intergranular precipitation, increasing the susceptibility to intergranular corrosion.

The resistance to pitting and crevice corrosion for stainless steels has been increased by the addition of rare earth elements. A rare-earth to sulfur-content ratio of about 10 to 50 produces the best pitting corrosion resistance. These rare earth elements produce this beneficial effect by altering the types and distribution of inclusions in these steels.

Construction Steels. The relationship between mechanical properties and the microstructure of C-Mn and high-strength, low-alloy (HSLA) steels has been studied at IM for several years. This research is quite similar in its objectives to the current HSLA steel program at the David Taylor Naval Ship Research and Development Center, Annapolis. The work at IM is done in collaboration with the Swedish Metallurgical Research Station in Luleå. The Ti-V grades of HSLA steels are of interest due to their excellent resistance to austenite grain growth at hot working and welding temperatures. The application of accelerated cooling (10°C/s) after hot rolling (from 950°C) can increase the yield strength for 12-mm-thick steel plate (0.01Ti-0.13V-0.02N) to above 500 MPa and produce a ferrite grain size of less than 6 µm. Swedish Steel is the first steel maker to have the capability for continuous annealing of steel strip (outside Japan). Thus, they are able to perform more complex heat treatments on steel strip than most other steel makers where box annealing of the coiled strip is used.

Roberts and his colleagues have developed mathematical models for the microstructural changes which occur during controlled rolling. This, combined with their knowledge of microstructure-strength relationships, is used to predict the loads and forces required for the rolling operation and to predict the final microstructure of the steel strip. They are concentrating on the development of Ti microalloyed steels because Ti is cheaper than V; but in order to successfully make Ti microalloyed steels, the steel maker must be able to consistently control sulfur and nitrogen in order to get reproducible properties (due to interactions between Ti and S or N). Swedish steel makers are more capable than most of accomplishing this, and thus they have a distinct incentive to develop these alloys.

The research in this department is good, and it is germane to the development of improved HSLA steels, a major goal in the US Navy's research programs.

Analytical Chemistry

The research in this department, headed by Dr. L. Danielsson, is on the development and application of new methods for the chemical analysis of metals. Optical emission spectrometry is currently receiving special attention. The department has an image dissector Echelle spectrometer. The most active research program is on surface analysis

using glow discharge optical spectroscopy (GDOS). In the glow discharge lamp the specimen surface is sputtered slowly (10 nm/s), and the optical emission signals are recorded as a function of time, producing a depth profile of the chemical composition. The detectability for most elements has been 0.01 to 0.1 percent, and compared to other surface analysis techniques (Auger electron spectroscopy or secondary ion mass spectroscopy), GDOS is simple and fast. Thus, it should find increased applications in the future. The technique is being used to analyze the oxide layers and coatings on metals up to 30-μm thick.

A research program on the improvement of analytical methods for the determination of trace elements in steels using atomic absorption spectrophotometry (AAS) is also in progress. The current work is focused on the determination of lanthanum in steel using the AAS in the flame emission mode.

Two other projects very relevant to the development of improved steel alloys are investigations to develop analytical methods to determine the free (noncombined) nitrogen in steel and to analytically separate soluble from insoluble aluminum in steels.

Current research on the improvement of steel alloys includes the determination of the role of impurity elements and alloying elements (added in very small amounts) on the strength and fracture properties of these alloys. In order to assess the effects of these elements, methods to accurately analyze the chemical composition of the steel both in bulk and very locally (or grain boundaries for example) must be available. The development work in this department has provided excellent experimental support in the area of chemical analysis to the rest of the institute by developing some very special and novel methods and apparatus for chemical analysis.

Structural Metallurgy

Cold formability (automotive industry), machinability (automotive and other industries), and elevated temperature strength (gas turbine industry) are all under investigation in this department. The major effort in this department is the study of continuous annealing of low carbon steels. This is in support of the new continuous annealing line for sheet steel at Swedish Steel's Domnarvet plant. Specific attention is given to the role dissolved carbon plays in modifying annealing textures, which in turn can improve the deep drawing properties of steel sheet used in automobile production. It has been discovered that increases in strength of over 100 MPa in the steel can occur during the paint-baking cycle of cold formed shapes. Current research is aimed at understanding this phenomenon in order to take advantage of it by developing the processing steps necessary to optimize this strength increase.

Sheet forming, cold forging, and wire drawing as influenced by microstructure are under investigation. The researchers have found that void formation at inclusions has a significant effect on the point of plastic instability during cold forming processes. During wire drawing the most critical parameter from the point of view of controlling "wire-breaks" has been found to be the back-pull stress on the entrance side of the die (contrary to the common belief that die geometry was the most important parameter).

Other projects in this department include creep and thermal fatigue testing, developing extrapolation techniques valid for the long-term service requirements of the Swedish power generating companies, testing of components made from powder metallurgy techniques, and isothermal low cycle fatigue testing of several different Cr-Mo stainless steels and nickel-base superalloys. This research is good, but very similar to work that is going on all over Europe. More information can be obtained by writing to Dr. A. Melander, department head.

Casting and Powder Metallurgy

This department, headed by Dr. O. Grinder, has research in five areas: (1) rapid solidification technology, (2) powder metallurgy, (3) surface properties and coatings, (4) continuous casting of steel, and (5) nonferrous metallurgy.

Many alloys, which would have undesirable properties such as gross segregation and embrittling phases if produced by standard melting techniques, have very desirable properties if rapidly solidified (10^5 °C/s to 10^6 °C/s) from the melt. By rapidly solidifying the liquid, one can produce a highly supersaturated solid solution, and the formation of undesirable intermetallic phases and gross segregation is avoided because the rapid cooling rate severely restricts diffusion. At IM these materials are produced as ribbons by melt spinning (pouring the liquid onto a spinning, chilled, copper cylinder) and powders are produced by ultrasonic gas atomization of the liquid followed by quenching the droplets in an inert gas.

About 2 years ago Dr. Lans Arnberg began a SKr4 million per year research project on rapid solidification technology (RST) funded by the Swedish Board for Technical Development and Swedish industry. He is studying methods for producing rapidly solidified metals and also characterizing the bulk mechanical properties of products made from these materials. Cold isostatic pressing followed by sintering, hot isostatic pressing, or hot extrusion are all being evaluated as consolidation methods. Arnberg is investigating: (1) high-strength aluminum alloys, (2) high electrical and thermal conductivity copper alloys with higher elevated temperature strength than that possible with today's commercial alloys, and (3) corrosion/oxidation resistant ferrous alloys.

Much of this research is part of the COST 503 powder metallurgy research program. The results are being published slowly, however, as the Swedish government wants to capitalize on any technological advances that result from this research.

One experiment has been published (L. Arnberg, L.J. Lange, and N. Backstrom, "Rapidly Solidified Ternary Al-Mn-Cr Alloys," in the proceedings of the Fifth International Conference on Rapidly Quenched Metals, Wurtzberg, West Germany, 2-7 September 1984). These results are only preliminary and simply report the thermal stability of three different Al-Mn-Cr ternary alloys. All three were 5.4%Mn, but the Cr content varied: 2.7 percent, 4.1 percent, and 5.9 percent. Foils were produced by melt spinning and then annealed at temperatures ranging between 200°C to 500°C. The chemical composition of any observed precipitates was determined with a Vacuum Generator HB501 scanning transmission electron microscope, and transmission mode x-ray diffraction using a focusing Guinier-Hagg camera was used for lattice parameter measurements. The lattice parameter varies almost linearly with total concentration of Mn+Cr, which indicates complete solution of the alloying elements. However, transmission electron microscopy revealed that the alloy with 5.9%Cr had some massive grain boundary precipitates present before the annealing treatment. Upon careful examination these precipitates were also found to be present with 4.1%Cr, but not in the alloy with 2.7%Cr. The precipitates are some unknown metastable phase; their composition is 12%Mn and 12%Cr, which is not any of the known binary or ternary phases present at equilibrium for this alloy system.

The Al-5.4%Mn-2.7%Cr alloy exhibited the best thermal stability; it did not undergo any precipitation after 3 weeks at temperatures up to 250°C. At higher temperatures (Mn,Cr) Al_{12} precipitates formed in all three alloys.

Based on micro-hardness measurements, these alloys maintained most of the as-cast hardness up to temperatures of 250°C. The applications for aluminum alloys will be greatly expanded (connecting rods in internal combustion engines, for example) if aluminum alloys with thermal stability and high strength at these temperatures can be commercially produced.

This research is worth careful attention; the results will be published slowly, and they should prove to be very interesting.

Other projects in this department include: (1) the characterization and study of surface properties of steel with regard to their effect on painting, galvanizing, and other surface coating processes; (2) soft soldering of copper and copper alloys with particular emphasis on processes used in the electronics industry; and (3) the development of new lead alloys based on powder metallurgy applications and RST (applications include bearing materials and batteries).

Summary

IM is Sweden's leading center for metals research. It is the research arm of all of the Swedish steel industry. Sweden's reputation for producing steel of the highest quality is due (at least partly) to the research that is performed by investigators at IM.

The institute maintains state-of-the-art facilities for this research and attracts scientists from all over Europe (many of the people that I talked with were British). Many international collaborative research programs are in progress; the excellent instrumentation available at IM and the vast experience in ferrous metallurgy make IM a very attractive partner for steel research. Some of their equipment is unique--e.g., a particle analyzing scanning electron microscope, called PASEM. (This is a minicomputer-controlled Philips scanning electron microscope with three electron detectors and image memory which will perform automatic particle characterizations down to 0.2 microns). This equipment would be very useful in studying the effect of inclusions on the microstructure of steel weld metal, a topic of great interest not only to the US Navy, but one that is receiving attention worldwide.

3/20/85

THE TECHNION--ISRAEL'S PREMIER MATERIALS-RESEARCH FACILITY

by Kenneth D. Challenger.

The Technion, Israel's only institute for technology, is the country's center for materials-related research. It has 20 different departments devoted to all major fields of engineering and science, and over 70 percent of Israel's scientists and engineers have been trained at the Technion. At present the enrollment is over 8000, with about one-fourth of these involved in graduate studies.

The Materials Engineering Department is the largest collection of materials scientists and metallurgists in Israel. About 20 faculty and 30 graduate students are involved in many different phases of materials research. Some of this work is state of the art and very relevant to the US Navy's programs.

There is outstanding research on cold sintering of powdered metals, ceramics processing, surface coatings, rapidly solidified materials, diffusion bonding, hydride-based energy storage materials, and interphase boundary characterization in metals and semiconductors.

Often this research is performed in collaboration with scientists in the US as most members of the faculty seem to spend about 1 year out of 5 working in the US; the very liberal leave policy and low salaries in Israel are responsible for faculty members spending so much time in the US.

Cold Sintering

Professor E.Y. Gutmanas is studying the mechanisms of cold sintering. Cold sintering may be necessary in many instances to consolidate metal powders which have unique properties that may be altered by consolidation methods at elevated temperatures. Many new alloys are being produced by rapid solidification (RS) methods, which can create supersaturated solid solutions and metastable phases in powder form. Parts manufactured from these powders can be expected to have unusually high mechanical properties if the chemical homogeneity and/or the metastable phases produced during RS of the powders can be retained. Hot isostatic pressing or hot extrusion are often used to consolidate these powders, but the temperatures used in these processes can change the properties of the powder.

High pressure, cold compaction experiments have been performed by Gutmanas on many different materials. When the compaction pressure exceeds the flow stress of the powder, plastic flow of the powder particles leads to high densities (99 percent of the theoretical density) and good mechanical properties. He has found that the best properties are obtained from particles with irregular shapes (rather than spherical). For example, spherical iron powders compacted at 3 GPa had a rupture strength of only 10 MPa, compared to 100 MPa for similarly compacted irregularly shaped iron powders. This result is important because it indicates that powders should be made by the water atomization RS techniques (producing irregularly shaped particles)--rather than the other conventional RS techniques, which produce spherical particles.

Gutmanas has found that the mechanism of cold sintering (the interparticle bonding that occurs during the compaction) is diffusion that is assisted by the plastic deformation and enhanced by the mechanical destruction of any oxide film present on the particle surfaces. This breakup of the oxide layers creates new, chemically clean surfaces that readily bond by diffusion. Although the density after composition approaches the theoretical density, the porosity that remains is in a very undesirable form--elongated thin pores along the particle surfaces. The properties of the compacted materials can be further improved by heat treatment at low temperatures (0.35 T_m, or less, where T_m is the absolute melting temperature). This temperature must be selected to be low enough not to lose the advantages of the cold compaction methods--yet in some instances the temperature must be as high as 0.35 T_m in order to promote a change in shape of the pores and some reduction in the total porosity. Thus, the porosity remains after the heat treatment, but it is present as small spheres rather than elongated grain boundary cavities. The mechanism for the shape change of the pores is believed to be grain boundary and surface diffusion; and in addition to these mechanisms, Gutmanas has shown that the dislocations in the particles near their surfaces (because of the plastic deformation) climb toward the pore surface helping to close the pores.

There are many possible applications of this manufacturing process, including the production of metal-carbide, metal-nitride, and metal-metal composites in addition to the processing of RS powders.

Ceramics

D.G. Brandon (professor and head of the Israel Institute of Metals) has been

working on the development of ceramics for armor materials; unfortunately, he had other commitments during my visit, and the only project of his that could be discussed was a project on which Gutmanas is a coinvestigator.

This project has studied the effect of various heat treatments on the toughness of commercial 85 weight percent Al_2O_3, AD-85 (this is a low cost ceramic which contains an Al_2O_3 rich alumina-silicate glass embedded in a skeleton of crystalline Al_2O_3). By proper heat treatment they have improved the plane strain fracture toughness, K_{IC}, and rupture strength, σ_R, of this material. K_{IC} has been increased from 2 MPa $m^{1/2}$ for non-heat-treated material to over 8 MPa $m^{1/2}$ and σ_R increased from 225 MPa to over 410 MPa. These properties are found to be very dependent upon the heat treatment. The critical requirements in determining the best heat treatment are: (1) heat to above the glass transition temperature, and (2) cool rapidly (forced air cooling of 7-mm-thick samples). The mechanism responsible for the increased properties is *not* believed to involve microstructural changes (dissolution or formation of precipitates) as might be expected, because anorthite, $CaO \cdot Al_2O_3 \cdot 2SiO_2$, and cordierite, $2MgO \cdot 2Al_2O_3 \cdot 5SiO_2$, are present and do undergo dissolution and reprecipitation as a function of the heat treatment. The researchers conclude that the rapid cooling from above the glass transition temperature results in a compressive residual stress in the glassy phase and a corresponding residual tensile stress in the skeleton crystalline phase. This explanation is consistent with the observed changes in the fracture surfaces as a function of heat treatment; the high-toughness materials exhibited smooth fracture surfaces caused by extensive cleavage of the crystalline Al_2O_3, whereas the low-toughness materials exhibited a rough fracture surface with the fracture caused by crack propagation mainly in the glassy phase.

This strength and toughness developed in AD-85 are as good as the properties of much more expensive engineering ceramics such as silicon nitride, at least for temperatures less than 600°C. Thus, a new low-cost engineering ceramic has been produced by this research.

Several other research programs of interest are expected to last for a few more years: (1) ceramics for heat engines, (2) ceramics matrix fiber composites (applied research on compatibility between fibers and various matrix materials and processing methods), and (3) silicon nitride ceramics (applied research comparing various available grades of silicon nitride for cutting tools, ceramic bearings, wear, and heat engines).

Rapid Solidification

Perhaps the most significant discovery ever made by a materials scientist at the Technion has just occurred. Professor Dan Shechtman, while studying a rapidly solidified Al_6Mn alloy during his sabbatical at the US National Bureau of Standards, has discovered the existence of a crystalline material which exhibits *fivefold* rotational symmetry. When examined by electron diffraction in an electron microscope, these samples were found to produce point diffraction patterns having twofold, threefold, and fivefold symmetry with the angles between the axes corresponding to those of a icosahedral rotational symmetry--an inadmissible crystal symmetry, at least up until this discovery. They have shown that this phase forms by nucleation and growth directly from the liquid. Their first explanation for the observed electron diffraction patterns was multiple twinning, but electron diffraction experiments contradicted this hypothesis. The solidification structure was obviously cellular which indicates that the growth of the icosahedral phase is slow enough to permit diffusional segregation on the order of 1 μm (the grain size of this material). This phase is found to be only metastable, but resists transformation to the stable Al_6Mn phase up to 400°C.

This phase has symmetries intermediate between those of a crystal and a liquid; however, it differs from other intermediate phases in that it is both solid and has long-range orientational order. These results by Shechtman have been reported by *Physics Today* (February 1985).

Surface Modifications and Coatings

Professor J. Zahavi has hypothesized that it should be possible to plate materials in standard plating electrolytes but without an applied current or potential if the electrons required for the electrochemical reduction reaction could be produced by photogeneration using a laser. If the laser has sufficient energy (as calculated from energy band gaps in semiconductors or bond strength in polymers), it is theoretically possible to cause the emission of electrons from the irradiated material. Again in theory, these electrons should be available to complete the reduction reaction (plating) if the ions to be reduced are in contact with the irradiated substrate. Zahavi has at least partly confirmed

this theory as he has been able to plate pure elemental gold on various semiconductors and polymers using both gaseous and aqueous electrolytes and laser irradiation (no externally applied potential). Plating ranging in thicknesses from tens of angstroms to a few micrometers have been produced.

This plating is possible either with or without surface melting when one uses a Q-switched Nd:YAG laser with an emission wave length of 530 nm. The applications of this process are numerous, especially in the fabrication of semiconducting devices as no masking is required; the plating is limited to the region irradiated by the laser beam.

Zahavi started this work while on sabbatical at Wright Patterson Air Force Base, Dayton, Ohio. The research is continuing at Technion because the mechanisms of the processes are not fully understood as they are much more complex than Zahavi's original hypothesis. This is very novel and exciting work--while I was there, a team of Japanese scientists was eagerly reviewing the research.

Zahavi has many other topics under investigation. They include layered composite coatings by electrodeposition and deposition of particles entrapped in a metallic coating (for example, Mo_2S particles as a lubricant entrapped in a Cr-Ni corrosion resistant layer). For the work in these areas he has been given the Gold Medal Award by the American Electroplaters' Society for the best papers published in *Plating and Surface Finishing* for 1982 and 1983.

His work is very imaginative and worthy of collaboration and/or support by the US Navy.

Metal Hydrides

Professor Moshe Ron, head of the Materials Engineering Department, has developed (through years of research) methods to produce compacted metal hydrides with high thermal conductivity. These hydrides are in the form of a very fine powder which is contained in a porous aluminum. Interconnected porosity of about 30 volume percent provides for rapid thermal conduction (30 W/m-°C as compared to 0.5 W/m-°C for a fine compacted powder) and high hydrogen sorption rates.

Ron feels that these porous metal matrix hydrides (PMH) are suitable for use as hydrogen heat pumps. He has built a prototype of an air conditioner for a bus and is testing it in his laboratory. The waste heat from the exhaust gases is used as the high-temperature source for the heat pump. In this part of the cycle, the efficiency is conduction limited, and Ron has shown that this can be enhanced by using the PMH compacts.

However, in order to become competitive with conventional air conditioning units, the hydrogen yield of the PMH must be further improved. This can only be done by increasing the amount of porosity in the PMH. The best PMH materials produced to date have a cooling power twice that reported by others (250 W/kg of absorbing hydride versus 120 W/kg, the best reported prior to the PMH). This, however, is still short of the 1 kW/kg that Ron feels is necessary to be economically justified. The PMH materials have been shown to resist fracture during the thermal cycling (a major problem with other hydride materials). This resistance to fracture, the thermal conductivity and hydrogen sorption rates as a function of the fractional porosity, and volume fraction of aluminum matrix are the current topics of Ron's research.

Another use of the PMH materials would seem to be for the storage of high purity hydrogen as a fuel, though hydrogen is a very expensive fuel.

Interfaces in Solids

The properties of the interfaces which separate different solid crystalline phases and interfaces which separate different crystallographic orientations of the same solid crystalline phase (grain boundaries) often have a large effect on the overall properties of the solid. Segregation of impurities to these regions can result in a local concentration of these impurities orders of magnitude higher than the bulk composition. Professor T. Komem has been determining the characteristics of the interfaces that cause this segregation. Most of his recent work has been done in collaboration with IBM's T.J. Watson Research Laboratory, Yorktown Heights, New York.

Bicrystalline thin gold films containing 4- and 16-degree (001) tilt boundaries were implanted with Co, Cr, Pb, and Au at 40 keV to integrated fluxes in the range of 1 to 100×10^{13} ions/cm^2. Transmission electron microscopy confirmed that Co and Cr segregated to the tilt boundary whereas Pb--being totally immiscible in Au--segregated to free surfaces rather than the grain boundary. The elastic strain contrast created by dislocations in these low-angle boundaries disappeared after implantation with Co or Cr, but remained after implantation with Pb or Au. The degree of segregation to dislocations is related to the solute atom-dislocation binding energy which is related to the misfit between the solute

atoms and host (solvent) atoms. For these implanted atoms this misfit is -0.131 for Co, and -0.134 for Cr, and +2.14 for Pb. The reduction in the strain contrast surrounding a dislocation observed when Co or Cr segregated to the dislocation indicates that a delocalization of the elastic strain associated with the individual dislocation cores has occurred. This implies that the interaction energy between dislocations is decreased and that the elastic strain field associated with the dislocation will play a less dominate role in determining the behavior of the dislocation.

The main conclusion of this study is that impurity solute atom segregation at dislocations in low-angle boundaries causes a delocalization of the elastic strain of the dislocations, which in turn causes a restructuring of the boundary through a change in the elastic interactions among the dislocations that constitute the boundary. Komem points out that this result indicates that the mechanism by which impurity atom segregation affects grain boundary migration must be reexamined. It is generally thought that the binding energy between the segregated impurity atoms and the boundary cause a drag force to exist that resists any movement of the grain boundary. Komem's results indicate that this may not be true, but that a restructuring of the boundary occurs because of segregation, which alters the ease with which atoms move across the boundary, thus affecting the movement of the boundary.

In another study, Komem (and IBM investigators) performed experiments designed to determine the mechanism by which improvements in the current gain occurs in bipolar transistors when highly doped polysilicon contacts are used instead of metal emitter contacts. The microstructure of the polysilicon interface is being correlated with the electrical properties. The results of these experiments were expected to be published in *IEEE Transactions on Electron Devices* (May 1985). The conclusion of this study is that minority-carrier transport in a polysilicon-monosilicon junction is controlled by a highly disordered layer within 1000 nm of the interface. This layer is characterized by a very low minority-carrier diffusivity.

It is my opinion that, although Komem is a major contributor to this work, the research is directed by IBM, and thus the results of the studies will be available to the US without any additional collaborative efforts.

Summary

The Technion is the center for materials-related research in Israel. Most of the faculty in the Materials Engineering Department and in the Israel Institute of Metals are active researchers. For both professional and financial reasons, most of them work in the US during the summer and during their frequent sabbaticals. Thus, their research should be well known in the US. However, none of them are associated with or collaborating with any US Navy scientists. This is something that should be rectified as many of them are excellent scientists interested in topics which are also of interest to the Navy. Everyone mentioned in this article could (and probably would if given the opportunity) make valuable contributions to the US Navy's research efforts; this is especially true for Shechtman, Zahavi, and Brandon.

A few of these people will be visiting the US Navy laboratories in the next year as part of ONR, London's visiting scientist program. I hope that this will build relations between Israel's materials community and the US Navy.

Reference

Shecktman, D., I. Blech, D. Gratias, and J.W. Cahu, "Metallic Phase With Long-Range Orientational Order and No Translational Symmetry," *Physical Review Letters*, Vol 53, No. 20 (1984), 1951-1953.

4/3/85

Mathematics

NUMERICAL ANALYSIS AT PAVIA

by Charles J. Holland. Dr. Holland is the Liaison Scientist for Applied Mathematics/Computational Science in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on reassignment until December 1985 from the Office of Naval Research, Arlington, Virginia, where he is the Deputy Division Director of the Mathematical Sciences Division.

The Istituto di Analisi Numerica (Institute of Numerical Analysis) in

Pavia, Italy, is an important European center in basic and applied numerical analysis concentrating on differential equations and their applications. Professor E. Magenes directs the activities of 13 professionals at this center, which is funded by the Italian National Research Council (Consiglio Nazionale delle Ricerche [CNR]). The group is doing research on a wide range of topics, including free boundary-value problems for flows through porous media, mathematical problems in biology and medicine, theory and applications of mixed finite elements, and spectral methods. Rather than reporting briefly on each of the projects, I will concentrate on two particular projects at the center in which the researchers are doing both excellent work and breaking new ground. In doing so, I omit discussion of the research of A. Quarteroni on spectral methods and F. Brezzi on mixed-finite elements, which is also of very high quality.

Hysteresis Effects

Some very interesting research is being done by A. Visintin on the mathematical formulation and numerical approximation of physical systems modeled by partial differential equations coupled with constitutive relations representing hysteresis effects. (Hysteresis is a memory effect arising in ferromagnetism, plasticity, and other chemical and biological models.) Despite the potentially wide applicability of these models to physical phenomena, mathematicians in the West have not devoted much effort to these problems; however, in the Soviet Union M.A. Krasnosel'skii and A.V. Pokrovskii (1984) have published a book summarizing their research in this area over the last decade. In phase transitions, hysteresis effects correspond to nonequilibrium situations in which memory has to be taken into account.

A typical case occurs when a monotone increasing relationship $v=f(u)$ between two variables u and v for $a<u<b$ is replaced by a hysteresis loop. This loop consists of two curves f_1 and f_2 with $f_1(u)<f_2(u)$ for $a<u<b$. As u increases from $u<a$, the pair $(u(t),v(t))$ moves along the lower curve f_1 in the loop, while if u decreases from $u<b$, the pair $(u(t), v(t))$ moves along the upper curve f_2. The case in which f_1, f_2 are constant functions corresponds to a relay. For instance, this relay can represent the temperature-phase dependence for the solid-liquid transition. Then u is temperature with say $v = -1$ representing the ice state and $v = +1$ representing the water state. The hysteresis relationship accounts for supercooling and superheating effects.

The equations considered by Visintin are of the form (A) $u_t + v_t + Au = f$ or (B) $u_t + Au + w = f$, where A is a linear elliptic operator, and f is a forcing function, with suitable initial and boundary data and a constitutive relationship representing hysteresis effects at each point in the domain. For both (A) and (B), continuous and discontinuous hysteresis relationships are considered. In all cases, existence of at least one weak solution is established in an appropriate Sobolev space; additionally, a uniqueness result is established for problem (B) provided the hysteresis relationship is described by Lipschitz continuous functions.

The existence results are provided by means of time and space discretization, a priori estimates, and a limit procedure based on compactness. The numerical algorithms suggested by these existence results are considered in one-dimensional versions of the problem (A) and (B) with f=o, $Au=-u_{xx}$ and either a continuous or relay-type hysteresis relationship. In this approach, time is first discretized by means of an implicit Euler method; then a finite element approximation is used on the resulting elliptic problem. Convergence of the resulting nonlinear Gauss-Seidel algorithm has been established and has been implemented on several numerical test problems. Since the exact solutions to these problems are not known, one must be satisfied with the appearance of the solutions.

Electrocardiology

Another area of intensive research activity led by E. Magenes at Pavia over the last several years has been on numerical algorithms for inverse problems arising in electrocardiology. In Italy as well as other countries, automated instruments are used to measure and record potential body surface maps (BSM). Typically, about 250 potential values of the electric cardiac field on the human surface for about 400 time instants of the cardiac beat are obtained. It is felt that BSMs can provide diagnostic information which could not be obtained by conventional electrocardiograms.

Several direct and inverse mathematical modeling problems have been formulated at Pavia in order to best use the information content of the BSM. One inverse problem in terms of the potential is to calculate the potential distribution on the "heat surface" from

the BSM. In this problem, the human body D is considered an isotropic linear resistive conducting medium excluding a region containing the heart. At any time instant, the electric field can be considered quasi-static, and the volume conductor D is imbedded in an insulating medium (air) so that the normal derivative of the potential is zero on the boundary of D. The electrical conductivity $K(x)$ in the body is assumed known. In view of the quasi-static assumption, one arrives at the following inverse problem for estimating the potential $V(x)$ on the boundary of heart C: from knowledge of $V(x)$ at points on the boundary of D, and the equations $\mathrm{div}\,(K(x)\,\mathrm{grad}\,V(x)) = 0$ in D and $\partial V/\partial n = 0$ on the boundary of D, determine the potential V on the boundary of C.

The inverse problem, even in the presence of no measurement errors, is known to be very ill-posed since it represents a Cauchy problem for an elliptic operator. Several regularization techniques imposing smoothing constraints have been attempted for this problem (Franzone, 1984).

Numerical experiments have also been performed with experimental data using different geometries to test the validity of their methods. In one geometry an isolated dog heart has been placed in a cylindrical tank containing a physiological solution. Measurements were made on the tank wall for data in the algorithm and at distances approximately 0.5 to 1 cm from the heart to test the validity of the algorithm for this problem.

Significant progress appears to have been made so far, and this work, in collaboration with physiologists, is expected to continue until practical devices are developed.

Conclusion

Researchers at the Numerical Analysis Center in Pavia are doing innovative work in the modeling and numerical analysis of physical and biological phenomena governed by partial differential equations. The work discussed on hysteresis effects in partial differential equations and inverse problems in electrocardiology are two examples of a wide range of activities there that should have impact on the mathematical and scientific scene.

References

Franzone, P.C., "Some Inverse Problems in Electrocardiology" (Pavia: Istituto di Analisi Numerica, 1984 preprint).

Krasnosel'skii, M.A., and A.V. Pokrovskii, *Systems With Hysteresis* (Moscow: Nauka, 1983, in Russian).

Visintin, A., "On Hysteresis in Phase Transitions" (Pavia: Istituto di Analisi Numerica, 1984 preprint).

4/15/85

Mechanics

RESEARCH ON COHERENT STRUCTURES IN TURBULENT SHEAR FLOWS AT TEL AVIV UNIVERSITY

by Patrick Leehey. Dr. Leehey is the Liaison Scientist for Naval Architecture and Applied Mechanics in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on leave until September 1985 from the Massachusetts Institute of Technology, where he is Professor of Mechanical and Ocean Engineering.

Professor Israel Wygnanski of Tel Aviv University is concentrating on the experimental and theoretical investigation of turbulent free shear layers excited by combinations of pure tones. This does not mean that Wygnanski, who is Lazarus Professor of Aerodynamics in the Faculty of Engineering, has given up his studies of boundary layer transition--work for which he is very well known. His large wind tunnel with an elongated rectangular test cross section is actively being used with test plates installed vertically for such studies. However, his present interests are largely related to two other facilities, and it is this work which I report on here. Wygnanski is using quantitative experimentation coupled with linear stability calculation and computer graphic displays of streakline and vorticity evolution to provide new answers to organized behavior in turbulent shear flows.

Experimental Facilities and Instrumentation

One of the two facilities is a dual contraction wind tunnel with a splitter plate in the middle in which he can produce flows of two different velocities, creating a rather thin planar shear layer between them. He uses a flap driven by a piano wire stretched over two phase-matched voice coils to excite this shear layer. The flap is attached at the end of the splitter plate.

Another wind tunnel facility is adapted for the study of axially symmetric jet flows with swirl. He has developed extensive hot wire measurement capability. He makes his own anemometers and his own wires, and produces various types of hot wire rakes, both linear and axially symmetric.

His data-reduction system is in the process of evolution, and he suffers from some of the same complaints that others of us have experienced. His throughput rates are generally limited to 80 kilosamples per second, which is inadequate for up to 30 individual transducers. He currently is using a DEC 1155 system with a DEC 6-bit analog-to-digital (A to D) converter. This system has 16-bit architecture. He also uses an older DEC 1123 system--also 16 bit. He allowed a VAX-780 to be removed from the laboratory and placed in the central computation center. It was connected with his system by an Ethernet cable. This has not proved satisfactory as his speed of data transfer has been reduced by a factor of 20 due to the protocols in the Ethernet system. Apparently DEC has become aware of the deficiencies of their present A to D conversion systems and is coming up with a new system with a throughput rate of 300 kilosamples per second. For test facilities remote from the computers, there is a firm known as Fibronics near Haifa which produces a direct fiber optics coupling to, say, a VAX computer over a maximum distance of 300 m. The system costs about $10,000. Such a system might well overcome present throughput rate limits on transmissions between experimental facilities and their data reduction computers.

Results

In spite of these problems, Wygnanski has made very sophisticated use of his digital data processing capability in his experiments with both planar and axially symmetric turbulent shear layers. For the planar shear layer, phase-locked measurements have been made of the amplitude and relative phase of fluctuating velocity components, Reynolds stress, and vorticity relative to the oscillating flap both at the flap frequency and at its first subharmonic frequency. Averaging over many cycles of oscillating eliminates the high frequency turbulence from the data, retaining the organized structure evolved from the excitation. Streaklines and isovorticity curves are then constructed digitally from these phase-locked data. For the same experiments, smoke flow visualization is also used. Here illumination is strobed at in phase with the flap oscillation, and long time exposure photographs are taken. These compare very well with the streaklines computed from the phase locked velocity data.

Inviscid linear stability theory is used to compute both eigenmode shapes and growth rates from the mean velocity profiles. The eigenmode shapes compared very well with the phase-locked transverse amplitude and phase distributions. The growth rates predicted by theory, however, are substantially greater than those found experimentally.

Wygnanski is somewhat critical of recent interpretations of flow-visualization experiments showing pairings of adjacent vortices in a vortex street as being essentially a nonlinear dynamical process. He has, for example, excited his two-dimensional shear flows at a given frequency and its subharmonic, and has mapped streaklines and vorticity patterns both experimentally and computationally. Experimental patterns show what would appear to be nonlinear vortex pairing action. But almost identical results can be obtained from the theory, which is entirely linear, of the response of the system to the two frequencies involved. It appears, therefore, that linear stability theory can explain pairings for excited turbulent shear flows.

However, an important nonlinear effect occurs when a resonant condition evolves. This resonant condition is one of wave-number matching between response at a given frequency and that at its first subharmonic frequency. The process can evolve nonlinearly after the subharmonic has grown appreciably. What is not presently known is how the subharmonic is generated--unless done intentionally. (For similar results for boundary layer flows, see my article "Receptivity, Transition, and Chaos at Novosibirsk," *ESN* 39-3:95-99 [1985].)

Similar evolutions occur in the swirling axially symmetric jets with corresponding excitations. That is, one can induce a rotational mode, say clockwise, and then superimpose on it an axially symmetric excitation of double the frequency. When the resonant condition occurs, one then can get a strong counterclockwise response. These effects are most dramatic.

Conclusions

Wygnanski feels that he is getting to the core of the evolution of structures in shear flows that are turbulent but where the general broadband turbulence plays a negligible role in the excited shear flow process. Certainly his research is a remarkable display of sophisticated experimentation coupled

with excellent digital graphics and theoretical computations.

4/11/85

Physics

SPANISH UNIVERSITY RESEARCH IN PHYSICS

by P. Roman. Dr. Roman is the Liaison Scientist for Physics in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on assignment until September 1987.

Rapidly developing countries offer many surprises. Conditions and performance factors of research are no exception to this rule. American scientists often get a slanted picture, for at least two reasons. First, they generally follow developments only in their own specialty. Second, by the very nature of international scientific interactions, they usually meet only the very best, most favored, and "smartest" colleagues from abroad. Fledgling efforts, as well as big gaps in coverage of topics or lack of progress, can be easily overlooked. But in an age when international cooperation in frontier areas as well as in applications becomes more and more the concern of the American scientific leadership, including those in the Department of Defense, one needs a broader view and understanding of the picture in less-known yet talent-rich countries. This observation motivated me to write this admittedly impressionistic and very restricted review. (A more detailed survey, including references to documents going beyond personal observations, has been published recently as an ONR, London, report.)

Background

During a recent, 16-day trip to Spain I visited 10 institutions and talked to about 15 senior people, including some with governmental advisory or other related activities. The areas I discussed and studied were modern optics (primarily quantum optics and optoelectronics), lasers, some microelectronics, nonlinear dynamical systems (including chaotic phenomena), telecommunication, and artificial intelligence. This article reviews the general status, strengths, and weaknesses of research I became aware of; the following article and the one on page 318 are, in contrast, regular scientific reviews on two selected areas.

Two important points dominate the picture. The first is that, even as late as 5 years ago, Spain invested only 0.3 percent of its gross national product in research and development, much less than Italy or Yugoslavia, for example. The second observation is that (with completely negligible exceptions) all universities and research institutes are government-run, and their personnel have civil service status. In addition, private high-tech industrial research is practically nonexistent, primarily because most big industrial establishments are subsidiaries of foreign enterprises.

A further interesting phenomenon is that, accelerated by new university laws, there has been an enormous migration of leading university scientists to Madrid. Even Barcelona lost some good people. One sad consequence of this is that although provincial universities were rarely competitive with those in Madrid and Barcelona to start with, they used to have good groups in special areas. These groups seem to have disappeared now; the members are leaving and modern equipment is going unused.

University Research

Of course, in contrast, institutes of higher learning in Madrid (and to a lesser extent in Barcelona) became mammoth establishments and, in any case, are primarily meant to be instruments of mass education. For example, the main all-purpose University of Madrid (called Complutense and of Renaissance origin from the town of Alcalá) has about 125,000 students and several thousand instructors; and, because it was overflowing, a new university (Autónoma) was built 15 miles outside the city, accommodating another 35,000 students. In addition, there is a Polytechnic University, an Industrial Technology Institute (in loose association with the former), and several special-purpose colleges. One unusual institution needs special mention: the National University for Instruction at a Distance ("Open University"). It provides advanced-level undergraduate education for nearly 100,000 people in the country (except in Madrid). The students are almost exclusively mature people who already have a degree and want to retrain in a new area, most likely a high-tech field.

Physics research is done at all these universities, but high quality is associated only with the Complutense, the Autónoma, and, surprisingly, the Open University. The research at the

Open University is strong because the scientists do not have students on the campus and thus have a more flexible and less overcrowded schedule than their colleagues at the other universities. Actually, to cope with the distractions of high teaching loads and student-overcrowded campuses, many professors at the regular universities by mutual agreement often concentrate all their teaching load into one semester and take off the other, either for local research or very often to work at foreign institutions. Germany, France, Italy, the US are preferred places of pilgrimage, and lasting research relationships often are built up that way.

Physics research, in the above-noted major universities, is done in a noncentralized format. You find independent departments of general physics, of experimental physics, theoretical physics, solid state physics, materials physics, statistical physics, optics, and electro-physics, each with a full professor as head and an independent budget. There is generally little cooperation between the physics departments, even though people know each other well from committees, which often cut across universities. Each department may have several special-focus groups. Unfortunately, these are often too small and may even consist of a single professor with, say, two doctoral and two to three pregraduation (diploma) students. In general, individualism is an overwhelming characteristic of physics research. Much too often one meets a truly outstanding, even highly productive, researcher who, because of the unfavorable infrastructure, is unable to (or sometimes does not care to) build up a strong group. Graduate students rarely stay on after earning the PhD; university life has not been made sufficiently attractive to them. It is difficult to see where they go since, as I mentioned, there is only very little private-industry research. It appears that these highly trained people get well-paid employment in private enterprise but are overqualified for the routine work they do and soon lose their research potential.

Equipment support and computer facilities are rather poor. This explains why theoretically oriented research is, generally speaking, superior to experimental work. But it would be a mistake to think that equipment and instrumentation are always the crucial factors. For example, in the fields I looked at more closely, the Autónoma in Madrid is much better equipped and has more modern facilities than the Complutense or the Open University; yet the level of research is much higher at the last two. The nonlinear dynamics group of Professor Manuel Velarde, the optics department of Professor E. Bernabeu, and the mathematical physics group of Professor J. Galindo deserve special mention.

In Barcelona there is, again, the Central University with about 55,000 students and, 25-km away, an overflowing Autónoma University with about 15,000. The Polytechnic University is also strong (perhaps 8000 students) and has a special semi-independent, research-oriented graduate school (Escuela Superior) system. I had the impression that better facilities, equipment, and people with leadership qualities are more visible in Barcelona than in Madrid. It may also be relevant to note that Barcelona's Autónoma and the Polytechnic University are designated as regional Catalán institutions. Since in Barcelona I deliberately concentrated on artificial intelligence work (see the article on page 318), I saw too little of other fields to be able to name outstanding physics groups.

Government Research

Even though I am reviewing primarily university research, it is unavoidable to mention, with much respect and approval, both basic and applied physics research that is carried out in the centralized government research laboratories, under the aegis of the Consejo Superior de Investigaciones Cientificas (CSIC). Founded (perhaps surprisingly) in the 1940s, this is a network of special-purpose research centers concentrated in Madrid but with several laboratories in various provincial cities. Generally speaking they have better equipment, more up-to-date instrumentation, and certainly less harassed researchers than the universities. Groups form easily and develop well. Graduate students can do thesis work at these institutes (but get their degree from some university). As an example of excellence, I should mention the Institute of Optics and the Institute of the Physics of Materials in the big conglomerate of government institutes in Madrid. Curiously enough, even in these front-line institutes, one may find a few labs which seem to have petrified decades ago. But the spirit, as well as the direction, is forward-pointing. Another peculiarity I observed in connection with the CSIC institutes is that presently there is practically no cooperation with the universities--despite the fact that employees at both types of installations are civil servants and are funded from the same ministry, so that there cannot be

administrative obstacles. An interesting and highly effective exception I saw is the Instituto de Cibernética in Barcelona, which is cosponsored by the Polytechnic University and the CSIC.

A most encouraging new development, resembling strongly the current US effort of building up a university-industry-government system of research partnership, ought to be noted. Steps are now in progress to bring into life a strong national Spanish research effort in microelectronics which would be based on a cooperation of two government research centers (one in Madrid, one in Barcelona), several universities, the Spanish telecommunication organization (Telefonico) and the American AT&T. It is expected that smaller firms will join in too. This effort is considered by many leading scientists as a first example of future, organized nationwide efforts.

Conclusion

It is not easy to summarize the picture I gained. Perhaps the most striking aspect of the scene is its unevenness and the many extremes. I think there is here a good opportunity for the American research community to explore building strong contacts with outstanding and front-line Spanish physicists. However, this should be done selectively, making sure that connections do not remain on the person-to-person level but lead eventually to the building of strong *research groups* that can perpetuate themselves and assure broad-based, high-quality work in the nation of an important ally.

2/20/85

MODERN OPTICS, MICROELECTRONICS, AND THIN FILMS RESEARCH AT MADRID

by P. Roman.

Even laymen must be aware of the scientific progress in the fields of modern optics, optical materials with unusual properties, lasers of all kinds, and microelectronics. These are technical "miracles" in communication, data handling, and information processing; there are space spectaculars, supercomputers and microcomputers, wrist-watch TVs, biomedical-engineering marvels, electronic warfare and countermeasures, and plans for an integrated, multilayered, partly space-based antimissile system.

But it should be emphasized that the spectacular successes in the construction of devices ("gadgets") and stupendous systems based on them did not, could not, come about by pure engineering "tinkering." Long and deep-probing research regarding the fundamental physical laws and the basic properties of matter under unusual circumstances are the prerequisites of such progress in practical applications. Moreover, this research has both laboratory (experimental) as well as theoretical aspects.

Now, it is obvious that much of the swift technological progress takes place in the countries of highest industrial potential. But basic research often needs fewer and less expensive resources and relies sometimes to a greater extent on inventive individuals than on large groups. It is, therefore, quite important for the US scientific community to obtain reports on basic research areas pursued in developing or rapidly changing countries. The physics background (if not all the experimental techniques) underlying modern quantum optics, optoelectronics, and the preparation, behavior, and modification of thin films or layered microstructures is often quite similar; this article discusses some of the favorable impressions I collected in this coherent area of physics during a recent stay in Madrid. (The preceding article presents a general review of the external circumstances and infrastructure of Spanish physics research.)

Relevant and innovative research, as well as interesting plans for future developments in the areas outlined above, is done at the Department of Optics of the Universidad Complutense, the Department of Optics and Structure of Matter at the Universidad Autónoma de Madrid, the Department of Fundamental Physics of the Universidad Nacional de Educacion a Distancia (UNED), and the Institute of Optics as well as the Institute of Materials Physics of the Consejo Superior de Investigaciones Cientificas (CSIC), the central government research council. These are places to watch in the future.

Optical Bistability, Fiber Research, Lasers

The most prestigious and coveted optics chair in Spain is at the Universidad Complutense. Its present holder is Professor E. Bernabeu, who previously organized and led a successful optics group at the University of Zaragoza. Less than 3 years ago he took over at Complutense; he has now assembled a good crew of 32 researchers (about half have

doctorates). Bernabeu is a dynamic person, chairman of the Spanish Optical Society, advisor to various governmental and university bodies, and skilled in turning such connections to his institute's advantage.

His own special research group consists of 12 people. Currently they have two major thrusts: optical bistability and fiber studies.

In the first area--so promising for optical memories, amplifiers, and logic circuits--Bernabeu and colleagues just concluded a project on the parametric dependence of the transmitted intensity in optically bistable Fabry-Perot devices. (The work was supported by the national Comisión Asesora de Investigaciónes Cientificas y Técnicas.) In this, the most common of bistable devices, the scientists analyzed the dependence of the transmitted amplitude on three parameters: the frequency of the incident radiation, the transition (resonant) atomic frequency, and the length of the cavity, keeping other parameters (including the input amplitude) fixed. They included both absorptive and dispersive contributions and arrived at a cubic state equation which, for the first time since such investigations were instigated, they could solve in the mean-field approximation. Thus, they obtained an explicit *analytical* expression for the transmitted intensity. Special cases of the solution offer new possibilities for optical switching/memory devices. For example, they found that under some circumstances very small (less than 1 percent) variation of the incident amplitude about a critical value will suffice to allow or block any jump of the output intensity. In other circumstances, small intensity variations may also serve to delete any previous codified information and cancel the initial memory. Current work is now aimed at obtaining quantitative analyses when additional parameters are included.

As is obvious from the example just cited, currently the bistability work is entirely on the theoretical level. But Bernabeu has strong assurances from the government that funds for extending the work into experimental research will be set aside in the foreseeable future.

The second major research focus of the Bernabeu group is on purely experimental work studying basic physical properties of optical fibers, so crucial for effective and reliable optical communication. Their current concern is dispersion studies. The researchers set up an interferometric system for this work. They use an ellipsometer system (previously developed in another context by Bernabeu's people) with which they determine the Moyer matrix by means of a series Fourier-transform procedure. Their unusually high-precision results recently earned much acclaim in France.

Future plans include research in the rapidly developing area of fiber sensors (especially fiber gyroscopes.) While many other institutes work along these lines as well, the scientists believe that combining more-or-less known approaches with their special ellipsometer work may lead to unique results. They are seriously interested in cooperating with the US in this area of considerable defense interest.

Bernabeu is very proud of his research group, and confident of its future. They already have a fine publication record (up to 10 papers a year in international journals), and Bernabeu believes his people could become an internationally pioneering group within 5 years. It would be worthwhile to keep an eye on them!

Within the Optics Department, I found one other research group that should be mentioned--partly because consistently good work is being done there and partly because a "push" could help. The laser group of Professor J. Guerra consists of five people, but all associates are students. Several, perhaps too many, aspects of laser experimentation are pursued. As far as I can judge, the truly original line is on gas laser development. While much of such work is now classic knowledge, the defense R&D community in the US still has an interest in new ideas. One possible focus is the improvement of transversally excited atmospheric pressure (TEA) lasers. Guerra used identical discharge chambers to study CO_2, CO, N^*, and N_2-based TEA lasers. By employing a sandwich configuration (between two glass plates) he obtained very reproducible behavior with substantially better stability than so far known. In addition, he is now reporting the achievement of subnanosecond pulses. In another configuration, where a tube with a changing profile was used, respectably high peak energy, up to 1 J/cm, was observed.

His most recent and probably most noteworthy research focuses on a fast and very stable N_2 transversally excited low-pressure laser where the discharge (after preionization by charges on the glass surface) takes place throughout the cavity, and its width is limited by the dielectric walls. His major goal was to study in very great detail the optical characteristics of the discharge, performing the measurements in the far field of the output radiation. The distribution of the output power through the width of the laser beam was found to

be symmetrical and very homogeneous. However, unlike other researchers, Guerra also observed a new and unusual dependence on the nitrogen pressure. Specifically, he noticed that at a low pressure the laser spot was only a line, but as the pressure increased, the spot divided into two principal lines, with the gap increasing with the pressure. Some secondary adjacent lines in the spot were also observed. This new phenomenon may have negative effects on the N_2 laser operation. In subsequent, purely theoretical work, Guerra formulated a simple model and used his experimental data to obtain information about amplification and refractive index distribution in the plasma, noting that this is essentially an inverse source problem.

Optoelectronic Phenomena and Crystal Growing

The Department of Optics and Structure of Matter at the Universidad Autónoma de Madrid is headed by Professor F. Agulló-Lopez. The department grew from a solid-state group which did good but not always pioneering work on point defects that were studied by optical and electrical methods. Interest turned rather naturally to "hot" technological problems connected with materials like $BaTiO_3$ and $LiNbO_3$, examining the physical basis for their use in optical devices such as active optical waveguides. More recently, the group scored international recognition by their continued work on the physical basis for the behavior of optical and microelectronics materials in phenomena such as photorefractivity, optical bistability, and phase conjugation. Needless to say, these loosely connected topics reflect the past of the group and are, to a large extent, theoretical studies. However, with the full support of the university authorities the department is now initiating a new 3-year plan which will lead them right into the center of proper optics, with immediate technical applications. It is for this reason--the group's well-prepared transition into a prominent role--that I wish to report on some initial and developing work.

There are four research activities developing:

1. In cooperation with industrial R&D groups, Raman spectroscopy is employed to study and improve superlattices, a truly hot area in future submicron quantum electronics. Impurities in alkali halides are also studied by Raman spectroscopy. In this area the group already has an edge on similar research by competing European institutes.

2. With increasing government support, a luminescence group has begun to use its expertise in the study of color centers (and impurities) in various crystalline materials. This has obvious implications for the current US Office of Naval Research (ONR) accelerated research initiative (ARI) in color center lasers, a serious competitor for semiconductor diode lasers. One example of the work proceeding in this direction is a just-published paper by Agulló-Lopez and colleagues on defects (and color centers) induced in pure and doped $LiNbO_3$ by means of x-ray irradiation and thermal reduction.

3. Nonlinear wave mixing electrifies a good many group members. First, in cooperation with the French École Normale Supérieure they began work on four-wave mixing to achieve phase conjugation. (For some background on this topic, see *ESN* 39-3:101-105 [1985] and *ESN* 39-5:211-217 [1985].) But more exciting is their planned project on light amplification by photorefractive beam coupling. This is essentially a two-wave mixing process. In the surface layer of a suitable nonlinear optical material, optical fringes are produced which, in turn, cause electrical (charge) fringes inside the slab. Under favorable circumstances there is an appropriate phase shift which induces nonlinear coupling, and light amplification occurs. Obviously, such a device could play a revolutionary role in optical fiber communication, where it would obviate the need for first converting (at each relay station) the optical signals into electric signals, amplifying these, and finally reconverting into optical signals. It is known that work on such direct optical light amplifiers is being done in the USSR.

4. One constant (and presently reconstructed) resource of the department is its crystal-growing laboratory, under the direction of Professor J.M. Cabrera. The lab is equipped with all types of single-crystal growing equipment--some of it on the scale of large-volume production--obtained, indeed, as a contribution from industry. The reputation of the lab is exemplified by the fact that recently the European Center for Nuclear Physics Research (CERN), commissioned them to develop a method for growing giant $Bi_4Ge_3O_{12}$ crystals that will be used for x-ray detection. Cabrera's people tried to use the heat exchange method but they found that it is too sensitive for large-scale industrial work. Currently they are modifying a Czochralski machine (with a radio-frequency heated

crucible) and hope to achieve CERN's goal for reliable, faster, and cheaper growth.

Another successful growth procedure, developed to perfection in this lab and, apparently not used successfully elsewhere, is the production of large and very high quality $Bi_{12}GeO_{20}$ crystals which have excellent photorefractive properties (these will be used in the light amplification experiments describe[illegible] ve.)

[illegible]s, the group is in transition and has made a good start. It certainly deserves the attention of the US research community.

Nonlinear Aspects of Laser Physics

The preceding article discussed the special status of research at the National Open University. Here I want to call attention to the remarkably well-organized research group of Professor M. Velarde, director of the Department of Fundamental Physics. This group has established itself in international circles, having connections with the US, Japan, Italy, and France, and it enjoys support from the Spanish government and the Volkswagen Stiftung. The group's central concern is the study of nonlinear dynamical systems, especially questions of stability and transitions to chaotic (turbulent) states. As is well known, this area of general thinking permeates now vast areas of front-line research, ranging from fluid turbulence to noise in quantum electronics devices, and is one of ONR's hotly pursued ARI topics. I cannot report in this article about all the special research topics actively followed in Velarde's group. (In a future *ESN* article, Dr. Patrick Leehey will review the group's work on fluid mechanics.) But to give a flavor of their approach, I will summarize some unusual results found by Velarde and Dr. J.C. Antoranz, in cooperation with younger researchers, in the area of laser behavior.

To put the work into a broader perspective, let us recall that systems which are driven far from equilibrium conditions can exhibit spatial and/or temporal patterns which show dissipative structures. These lead to interesting, collective states, covered by the catch-all term "synergetic behavior." The new states (whose appearance is essentially like a phase transition) can arise either "softly" (continuous transition) or through "hard excitation" (discontinuously). A specific case of nonequilibrium transitions is the appearance of multiple steady states which, in the particular instance of laser systems, permit the celebrated phenomenon of optical bistability referred to repeatedly in this and other *ESN* articles.

Through a carefully defined and rigorously solved theoretical model, the Velarde-Antoranz group demonstrated some time ago that sufficiently long population decay times and sufficiently short dipole decay times in a single-mode laser with a saturable absorber will permit, in the form of a hard-mode sustained relaxation oscillation, the occurrence of passive Q-switching (i.e., the buildup of the population inversion to a very high level followed by a swift and energetic discharge). In this work they also called attention to the danger of a straightforward extension of the equilibrium phase transition picture to dynamic nonequilibrium problems. In more technical terms they pointed out that even though one may find a Landau potential with extrema at different steady states, to know that a state corresponds to a minimum is not enough to assess its stability. (One must also show that the Landau potential is a Lyapunov functional of the system.)

In a follow-up paper, the authors extended their study to a range of parameter values where a nontrivial role may be played by the phases (which were previously ignored.) They found the (to me, at least) surprising result that under such circumstances, the hard-mode sustained Q-switching may be accompanied by coexistent soft-excited oscillations, and this leads to bistable limit cycles. The novelty relative to previously known results is that the limit-cycle behavior exists not only between two softly excited oscillations, but also between soft- and hard-excited oscillations. Although the authors do not discuss practical applications, it is likely that such considerations should affect laser technology developments.

The Velarde group is eager to establish working contact with ONR researchers, and I believe that this would be beneficial for both parties.

Optical Memories, Laser-Thin Film Interactions, Color Coded Imaging

CSIC's "Daza de Valdés" Institute of Optics, under the general direction of Dr. A. Corróns, is one of the oldest and internationally reputed research centers within the over 40-year-old chain of CSIC institutes. It employs 29 permanent, PhD-holding scientists, a varying number of short-term visiting researchers, and eight graduate students. It has seven informally interacting research groups: optical properties of solids, image processing and vision, holography/frequency filtering,

radiometry/colorimetry, atomic spectroscopy, molecular spectroscopy and chemistry, and solar energy.

In my view, the first group, under the leadership of Dr. Carmen Ortíz, is conducting effective, innovative, frontline research which will interest US researchers working not only in optical memories, surface modification, and laser damage studies, but also in the area of thin film technologies--all these having multiple high-tech applications. (Actually, Ortíz already has contacts at the Naval Research Laboratory and had ONR support in the past.)

The general goal of the Ortíz group is to understand the structure and basic physical properties of a wide variety of thin film materials (as well as bulk samples) and to modify their physical properties so that they become suitable for up-to-date technological applications, including optical memories and optical detection devices. The typical work of the researchers involves creating defects in thin films by laser-beam interactions, producing new materials by using very short laser pulses on multimaterial layers, and testing with laser and other technology the optical properties (such as reflectivity and transmissivity at different frequencies) of the samples produced. In other studies they create defects in bulk material with x-ray irradiation, ion implantation, or neutron irradiation and test by optical methods the nature of these defects. Of course the practical purpose of these basic studies is to have high-tech results like information storage devices, and work in this direction is done by many industrial enterprises too. But, Ortíz told me, "They may be able to fabricate a device faster than we do, yet they don't know why and exactly how it works." The basic-research exploration of these details is the only rational way not only to eventually arrive at cheap and reliable devices but to also control factors such as a good signal-to-noise ratio.

At a recent international conference in Madrid, Ortíz presented a paper which went far in showing progress in the creation of thin film materials that can store optical information at room temperature. The talk described the creation of Ge_xTe_{1-x} films in a triode-sputtering system by codeposition from two independently polarized Ge and Te targets. This technique differs significantly from the work of other research centers that used evaporated films. The Ortíz films (24- to 30-nm thick) were grown onto glass substrates. Multiple probing studies showed superior properties in the storage system and a favorable relation between structural and ablative conditions.

In a report to a 1984 thin-solid-films conference in Sweden, the Ortíz group reported on the not-well-explored topic of the interaction of nanosecond-pulsed high energy laser radiation with thin films. The laser mixing produced in a multilayered structure was studied in GeAl (good metal) and GeTe (bad metal) systems. The layered thin films were produced by DC triode sputtering or by electron gun deposition, with independently polarized sources. Successive layers (2, 4, and 6), each with a thickness between 100 and 1000 angstroms were grown. These structures were then treated with multiple pulses from an excimer laser (λ = 284.2 nm), and subsequently the layer distribution and composition were studied by nuclear Rutherford backscattering, scanning electron microscopy, and x-ray diffraction so as to obtain previously unavailable data on the mixing results.

These two examples show that the group is doing mature, multidisciplinary work with contemporary equipment.

A newly started research line aims at manufacturing three-component thin films. (It appears that, so far, no other group has gone beyond the two-component structures.) The idea is to combine materials with high-quality properties in *different* areas. A typical three-component film would have a "Te X Y" composition (not necessarily stochiometric). Here Te has good optical storage properties but corrodes easily; X (such as Ge) is an anticorrosion material; and Y (such as Se, Bi, As or some other low-melting-point material) makes the structure amorphous. Initial results are encouraging.

The work of Dr. J. Santamaría (the image processing/vision group) is another outstanding activity in the Institute of Optics. One of his interests, overlapping multiple civilian and defense applications, is optical pseudocoloring (or pseudocolor encoding) and color image enhancement. In his latest work (with two associates) he devised a new method to generate a family of color-coded images using holographic techniques. The method involves the introduction of three primary colors and thus overcomes a serious limitation of previous holographic techniques. The procedure is as follows. First, an image hologram of a black-and-white transparency is registered, which then is put in contact with a beam splitter, and the sandwich is illuminated by three partially coherent waves. One wave produces a positive image, a second wave makes an image with reversed contrast (the

negative), and the third image corresponds to the product of the positive and the negative. These waves are then coded in three primary colors. If one adds them, a color-coded image is obtained at the final image plane. The successful trials of the method demonstrated that the introduction of the third color in the product distribution increases considerably the color space zone that contributes to the coding.

In essentially unrelated work, Santamaría obtained dramatic color enhancement of transparencies with degraded colors. This he achieved by attenuation of the zero order component of the white light spatial spectrum. The attenuation can be done either simultaneously for the entire visible spectrum or through sequential exposures, each with a color filter and a predetermined attenuation.

Image processing experts at the US Department of Defense might want to contact Santamaría, who feels somewhat isolated despite his good reputation.

Microelectronics

The design and preparation of highly integrated and miniaturized electronic components and systems with a wide range of possible behavioral characteristics is a steadily growing area with crucial implications for all of modern technology. In view of the fact that the most industrialized nations of the world play an obvious leading role in this high-tech area, one may wonder whether the US research community may be able to learn anything new from workers in industrially less-developed countries. My visit to CSIC's Institute of Materials Physics Research convinced me that it would be a mistake to ignore work in this area that is done in "quiet corners." To start with, the director of the microelectronics group, Dr. J.L. Sacedon, told me that while Spain cannot expect to compete in *all* areas and would not develop a high marketing capacity in competition with, say, the US or Japan, the government found it imperative to develop the potential of manufacturing all electronics devices that are necessary to make their own, customary, non-high-tech products function in modern modes of operation and be competitive with foreign products. (Simple examples are autos, up-to-date communication equipment, household products, and toys). Within this framework, then, there is ample room for innovative, off the center of the road, yet potentially important advances. Also, since there is proportionally more work done in this area at the universities and government research labs than at industrial labs (virtually nonexistent), one might expect a more fundamental and basic approach than is customary in other countries. A good look around the labs convinced me of the validity of these views.

Sacedon's personally directed research group is particularly interested in electron beam stimulated oxidation (ESO) of various components. Not long ago they achieved an international "first" when they succeeded in producing several complete layers of oxide on a Si (111) 7×7 surface, while others managed only about a one-half monolayer. Further work was done on stimulated oxidation of GaAs; and, for the sake of pure surface physics studies, on Si and Al as well. The general goal is a direct integration of the oxide on a semiconductor surface. He also experiments with using the technique in more general contexts than oxidation--for example, for the preparation of masking.

He admits that the low rate of oxide growth makes the process not very suitable for large-scale industrial applications. However, he believes that in many applications one will not need to obtain a stoichiometric ratio and mere doping with oxide will suffice--which of course goes much faster. For example, he and his associates are using the ESO technique for oxide doping of GaAs in order to prepare a novel kind of metal-oxide-semiconductor device. This approach allows one to follow the growth during the process by means of techniques such as Auger spectroscopy, low energy electron diffraction, and x-ray probing, and thus to have high control over the fabrication process.

Sacedon notes that their ESO technique faces competition from laser-induced oxidation methodology. But he thinks that while the latter may be more satisfactory for mass production, in the fabrication of special-purpose, research-application-oriented devices, ESO may easily win out. Moreover, it may have advantages in allowing proficient single-step fabrication of integrated devices. In summary, one should realize that ESO allows for direct electron beam writing (as opposed to the more conventional mask-working processes).

Plans for the future are numerous. Sacedon wants to use his technique to put oxygen into PbTe single-crystals, which cannot be done well, it seems, by other methodologies. Next, he wants to study the lateral resolution of the ESO method in order to see if it could be used eventually for very-large-scale-integration technology. Since nobody appears to understand the physical mechanism of Si doping of GaAs, he wants

to study carefully the Si-GaAs interaction. The stimulating effects of silane (SiH_4) and the production of Si_3N_4 layers (which is a good dielectric and also a good barrier for oxidation) are also on the list of research projects.

The picture of the microelectronics research lab would not be complete if I did not mention briefly the unusually enthusiastic group of young researchers with Dr. F. Briones. To start with, they built a fine and versatile, research-oriented molecular beam epitaxy (MBE) apparatus. They use it primarily for learning studies, to achieve leading potential in this modern and most promising technology. But already they have employed their MBE apparatus to study new phenomena. In one study, for example, they explored the possibility of using SiH_4 as a cold source of Si dopant, during MBE growth of GaAs and $Al_xGa_{1-x}As$. In a very new, yet-unpublished paper, the group reports how they used H_2S gas during MBE growth of GaAs and $Al_xGa_{1-x}As$ as sulphur vector for n-type doping. Good mobilities were obtained for GaAs in a broad concentration range and no memory or contamination effects were observed. However, doping efficiency was low.

In summary, it is clear that basic physical studies predominate over immediate application-oriented efforts in this lab. But this may be, indeed, a strength rather than a weakness. Sacedon pointed out to me that, at least as long as the defense ministry is involved, transfer of basic research results to development and implementation may be quite fast in Spain. (A good example is the quick transfer of basic infrared-detector studies to applications by the military.) But this is not so with the private industry. Conversely, he believes that the US will be unwilling to facilitate technology transfer to Spain, except for restricted basic research. For this reason, he would enthusiastically welcome close links with the US Department of Defense community where the chances of mutual cooperation in application areas may be greater.

Conclusion

It appears to me that in selected areas of optoelectronics, solid-state physics, and basic physics research Spain can be favorably compared with many European countries. A period of uneasiness and aimlessness seems to have ended. Strengthening contacts between US researchers and their Spanish colleagues very likely would lead to mutual benefits.

2/13/85

Science Policy

CNRS--THE MOST IMPORTANT ACRONYM IN FRENCH RESEARCH

by David L. Venezky. Dr. Venezky is the Liaison Scientist for Chemistry in Europe and the Middle East for the Office of Naval Research's London Branch Office. He is on reassignment until October 1986, from the Naval Research Laboratory, Washington, DC, where he was the head of the Inorganic and Electrochemistry Branch and Associate Superintendent of the Chemistry Division.

The Centre National de la Recherche Scientifique (National Center for Scientific Research), or CNRS, is the largest organization and the most influential authority in directing and financing basic and applied scientific research in France. Under the authority of the Ministry of Research and Technology, CNRS has legal stature and financial autonomy as a state-funded scientific organization covering all scientific fields. Created in 1939, CNRS now boasts an annual budget near F8 billion (slightly less than $1 billion), 25,000 employees (9900 researchers and 15,100 engineers, technicians, and administrative personnel) in about 350 CNRS-operated units and 850 associated units. (The article on page 316 discusses an example of an associated unit.)

CNRS's mission was clearly defined by decree on 24 November 1982 as follows:

1. To evaluate and carry out directly or indirectly any research in the interest of the advancement of science and of France's economic, social, and cultural progress.
2. To support transfer of technology.
3. To develop scientific information, encouraging the use of the French language.
4. To contribute to training for and through research.
5. To set national scientific policy in light of current and future trends in the national and international scientific situation.

The advancement of science and of France's economic, social, and cultural progress (mission 1) is clearly coupled to technology transfer, the application and government support of research

results (mission 2). As a consequence of the close association of research and application, the national scientific policy (mission 5) becomes the most important part of the CNRS mission and the most politically sensitive part of its activity. In the rest of this article, I will briefly summarize the administration of CNRS and its role in research, review the areas of current support, and discuss technology transfer, information transfer, and cooperative research.

Administration

CNRS is governed by an administrative board presided over by a scientist appointed by the French cabinet. In 1984 Claude Frejacques presided over an administrative council made up of working members from the Ministries of Budget, Industry, and Research and National Education. Of the other 16 members, four were chosen for their competence in economics; four were scientists (Jean Daussel, winner of the Nobel Prize in medicine; Raymond Castaing, a physician; a historian; and Jean-Maire Lehn, professor of chemistry); four were representatives from workers' unions; and four were CNRS staff personnel.

The scientific, administrative, and financial direction of CNRS in entrusted to the director general, who is appointed by the French cabinet and assisted by a secretary general and scientific directors who supervise the management of seven scientific departments, two national institutes, and four directorates (Table 1).

Table 1

CNRS Departments, Institutes, and Directorates

Scientific Departments

- Nuclear and Particle Physics
- Mathematics and Basic Physics
- Physical Sciences and Engineering
- Chemistry
- Earth, Ocean, Atmospheric, and Space Sciences
- Life Sciences
- Humanities and Social Sciences

National Institutes

- National Institute for Astronomy and Geophysics
- National Institute for Nuclear and Particle Physics

Directorates

- Application of Research
- Scientific and Technical Information
- International Relations and Cooperation
- Budgetary Programming and Forecasting

An advisory and assessment body, the National Committee for Scientific Research, continually assesses the results of CNRS activities and the quality of the work accomplished by its research teams and investigators. This group of 45 disciplinary sections, interdisciplinary commissions, departmental councils, program committees, and the CNRS Scientific Council is responsible for analyzing the overall French scientific environment and suggesting increased or new areas of activity.

The CNRS scientific council, chaired by the director general, sees to the consistency of the CNRS scientific policy as determined within each scientific department in conjunction with consultative bodies. On the other hand, the administration of the CNRS is decentralized throughout every region of France. Regional scientific delegates represent the CNRS at the local level and establish cooperation with local facilities to develop scientific projects in each region.

CNRS's Role in Research

CNRS defines the policy objectives of each scientific department within the framework of the national research policy which is implemented by various means. These include: research facilities operated directly by CNRS; CNRS-sponsored associated laboratories within universities (discussed on pages 316 to 318), *grandes écoles*, and other organizations; consortia of research teams and laboratories on a specific topic; specific research thrusts; participation in international scientific organizations operating unique instruments (for example, high-flux vector in Grenoble and the 3.6-m telescope in Hawaii).

CNRS Areas of Research

The broad extent of the CNRS-sponsored basic and applied research is summarized in Table 2. (For a more complete listing in a given department, write to CNRS at the address given at the end of this article.) Not listed in the table are a variety of interdisciplinary research programs covering energy and raw materials, the environment, scientific bases of drugs, prediction and observation of volcanic eruptions, oceanography, materials and technologies, labor, employment, and lifestyles.

Technology Transfer

CNRS pursues an active policy to assist industry and the growth of the French economy. When industrial managers need information concerning CNRS's research, the Research and Technology

Table 2

CNRS Basic and Applied Research by Departments

Nuclear and Particle Physics Department
Nuclear physics
Particle physics
Mathematics and Basic Physics Department
Mathematics and mathematical models
Theoretical physics
Atomic and molecular physics
Condensed matter physics, solid-state physics
Physical Sciences for Engineering Department
Computer science, automation, signal processing and systems
Electrical engineering, plasmas, optics, microelectronics
Mechanical engineering, fluid mechanics, and acoustics
Process and reaction engineering, heat transfer
Chemistry Department
Coordination chemistry and catalysis
Electrochemistry, kinetics, and photochemistry
Molecular organic chemistry and inorganic materials
Biological and therapeutic chemistry
Molecular and macromolecular chemistry
Earth, Ocean, Atmospheric, and Space Sciences Department
Astronomy and planetary environment
Ocean and atmosphere
Earth: physics, chemistry, and internal dynamics
Earth: history, structure, and external dynamics
Life Sciences Department
Structure, biosynthesis and interactions of biological macromolecules
Biology and physiochemistry of integrated macromolecular systems
Genetics and cellular biology: microbiology
Plant biochemistry and biology
Pharmacology and experimental therapeutics
Psychophysiology and psychology
Experimental and human physiopathology
Animal physiology
Humanities and Social Sciences
Anthropology, prehistory, ethnology
Sociology, demography
Legal and political sciences
Modern and contemporary histroy and civilizations
Linguistics
Philosophy, epistemology, history of science and technology

Data Bank refers them to competent laboratories for assistance. The technical problems faced by industry are often the subject of meetings held by the Industrial Relations Committee. The committee's topical groups consisting of researchers and industrial representatives jointly undertake an analysis of the problem and provide solutions or advice.

The transfer of research results to industry is implemented at the regional level by a network throughout France of *chargés de missions* for industrial relations. They ensure the interface between private firms and local laboratories in cooperative research contracts, manufacturing licenses, and establishment of businesses to complete the technology transfer. In addition, CNRS promotes the temporary exchange of researchers with private firms, consulting activities, and the training of future industrial engineers for research.

Training and Scientific and Technical Information

The CNRS mission to train engineers and technicians, train teachers, and create teaching tools is accomplished mostly by supporting high-quality research in the universities and financially supporting instrumentation acquisitions. The faculty members who work in such an environment provide well-educated and trained students to industry. Except for minor problems, the training process appears to be successful. A more detailed discussion of the education

programs is beyond the scope of this report.

Scientific and technical information is disseminated by CNRS through exhibitions, brochures, films, and open labs for all audiences but primarily aimed at young people. Multidisciplinary or field-specific bibliographic databases are created for research activities and industrial development. The publication of scientific books and periodicals is supported in many cases through grants. The CNRS itself published more than 160 books in 1983.

National and International Cooperation

CNRS has signed cooperative agreements with other large public research organizations, thereby allowing CNRS laboratories (operated directly or associated units) to work with other research organizations on projects of mutual interest.

CNRS's international cooperation in research is impressive. Their policy of international relations and cooperation is based on the desire to reinforce European collaboration by setting up a mechanism to encourage long-term postdoctoral exchanges, financing activities carried out in conjunction with Third World countries, initiating major coordinated research programs with the US and other industrial countries outside the European Economic Community, participating in many international societies and organizations, and keeping aware of scientific research trends in other countries. The statistics for 1983 (published in 1984) show (approximately):

- 2500 research months exchanged under 42 agreements with 33 countries.
- 10,000 visits abroad initiated by CNRS laboratories.
- 125 foreign researchers at the level of associated researchers.
- 2000+ young foreigners trained at CNRS laboratories.
- 200 international conferences sponsored by CNRS.
- 700 foreign researchers in permanent CNRS positions.

Summary

All aspects of basic and applied research in France are reviewed and evaluated by CNRS. The council/committee operation, assessment, and direction of CNRS is producing high-quality students and first-rate research that is being transferred to industry and strengthening the French economy. Most important are the satisfied researchers who are experts in their field of research and sought nationally and internationally for their assistance and cooperation in research. As in any large organization there are visible annoyances: political favoritism, jealousy between CNRS employees and teaching faculties, slow response to funding appeals, not enough funds, and overabundance of administrative reports. All of these problems are, I believe, familiar to any person in a similar funding organization, regardless of country.

For general information about CNRS, contact: Ms. Claire Giraud, International Relations, Centre National de la Recherche Scientifique, 15 quai Anatole France, 75700 Paris, France; telephone: 555 92 25.

4/19/85

R&D IN ADVANCED COMMUNICATION TECHNOLOGY FOR EUROPE

by J.F. Blackburn. Dr. Blackburn is the London representative of the Commerce Department for industrial assessment in computer science and telecommunications.

The Council of Ministers of the European Economic Community (EEC) agreed last December on a set of objectives for community actions in the field of telecommunications, including the execution of a development program covering the technologies required for establishing, in the longer term, integrated broadband networks. This action was based on their realizing the growing importance of telecommunications for the future development of the community's activities. The new program will be called RACE, for R&D in Advanced Communication Technology for Europe.

RACE, a precompetitive R&D effort with a specific objective, will rely on technology programs of generic character for the nontelecommunication-specific R&D; these are national programs in information technology and the EEC's ESPRIT program of research in information technology (*ESN* 38-5:248-252 [1984]). R&D topics offering opportunities for synergy between RACE and ESPRIT are well understood as both programs are coordinated by the same task force in the ECC Commission.

Rationale for the Community R&D Program

Telecommunications advances in the future will be shaped by the improved cost performance of electronic components, the growing need for broadband

communications, the emergence of optical technology, and the advances in software. Typical prices for integrated circuits have been dropping by 20 to 30 percent per year. And at the same time the density of information on a single chip has been increasing at a comparable rate. Increased integration and component price reduction work together to improve the price performance of systems.

The need for broadband communication is increasing because of the amount of data that must be manipulated in image processing, simulation, and other applications with high demand for data. The developments in fiber optics offer the possibility of cheap, high-capacity transmission. Its main advantage is the immense capacity of the optical fiber at a system price per unit cable length of about that of conventional copper cables. Devices are needed to transmit, couple, amplify, and receive the light signals being carried. Interfaces with the electronic parts of the overall system are required, and therefore optoelectronics technology will be a major element in such systems.

Optical fibers to some degree complement and to a degree compete with satellites as carriers. Satellites can generally be expected to dominate where large or remote areas need to be covered. Optical communication may dominate the regions with high user density or a high rate of traffic.

The convergence of communications and computer technology has led to a single technology becoming central to a wide range of previously distinct sectors and applications. At the same time the variety of uses of this technology is rapidly increasing. This has accelerated the rate of change in the telecommunications sector. As technological change accelerates, lead times for the development of new products are necessarily reduced.

The broad objective of the EEC--"Community-wide evolution towards integrated broadband (IBC) by 1995, taking into account the evolving integrated services digital network (ISDN)"--provides an objective for R&D in telecommunications.

The IBC scenario is expected to include local and national subnetworks and will evolve from or subsume the present services and network services. The eventual scenario is expected to be the creation of a Europe-wide broadband network infrastructure capable of supporting a wide range of customer and service providers. This requires the complementary customer and service provider terminal equipment and creation of the appropriate standards needed to achieve a complete service offering to the customer.

The targets of the IBC are an experimental system by 1990 and a standardized operational system by 1995. The operational system would mean the Europe-wide introduction of broadband services by the telecommunication operators and service providers in the member states, based on common standards and regular products of the telecommunications, terminal, and service industry.

The technology will be predominantly fiber optic transmission, down to and perhaps including customer premises. All switching will be digital.

Services will include all business and domestic telephony, data services, and video services. The most demanding service in terms of bit rate is high definition TV and, possibly, high-quality videophone applications.

Objectives and Scope of RACE

The objectives of RACE are as follows:

1. RACE should address long lead-time R&D issues at the precompetitive stage.

2. RACE should ensure that the anticipated IBC Scenario is progressively clarified in order to influence effectively the scope and direction of the R&D.

3. RACE should lay the technological basis for European IBC, while enhancing the capability of the indigenous industry to compete effectively on world markets.

4. RACE should seek solutions that make new broadband services economically feasible early on and traditional services more economical to provide.

5. The program must also address those shorter term R&D issues that are necessary to underpin the evolution of IBC from existing networks and services.

6. The program content must be carefully checked with respect to synergy and overlap with related actions, in particular ESPRIT, national programs, and the cooperation of the telecommunication operators in the framework of the Cooperation for Scientific and Technical Research program.

7. RACE must address those R&D issues related to IBC which offer significant advantages when carried out on a Community scale.

The phasing of RACE in the context of IBC evolution is divided into a definition phase followed by two 5-year development and implementation phases.

The definition phase (1985-86) will execute initial work as required to

focus the R&D work of the main program accurately toward future functional requirements of IBC and carry out exploratory R&D on key items of agreed urgency. Phase I (1987-92) will emphasize the technological development required to initiate demonstrations of IBC introductory systems by 1990. Phase II (1992-97), depending on the results of Phase I, will develop the more advanced methods and techniques needed to enhance and extend general IBC demonstration, and hence IBC itself, beyond 1996.

In the area of software R&D it is expected that RACE can benefit from progress in software technology in national programs and in the ESPRIT program.

The cost over the duration of the definition phase is expected to be 42.9 million European currency units (1 ECU = $0.72), of which 22.1 million ECU will come from the budget of the Communities and 20.8 million ECU will come from national budgets.

4/15/85

News and Notes

COASTAL BATHYMETRY AND CURRENTS IN TIRAN STRAITS OBTAINED FROM LANDSAT DATA

One of the major problems facing Earth's scientists in the use of remote sensing data is that of automatically eliminating noise from various sources. At the University of Tel Aviv, Faculty of Engineering, Professor Norman Rosenberg has been developing a number of filter algorithms that can remove both artifact and other noise sources from LANDSAT scenes of coastal areas. Promising results have been obtained in an application of these filters to certain regions of the Israeli frontier coastline.

The basic goal has been to deduce useful bathymetry data for mapping sediment flow associated with various subsurface currents. Classically, the satellite observes scattered illumination associated with four principal sources: the atmosphere, the land and water surface, the water itself, and the sea bottom. Maximum sea-bottom depths that can be detected in clear water are typically between a few to several tens of meters in the LANDSAT data. Sensitivity to scattered signals depends also upon solar elevation angles due to nonuniformity of the back-scattered signals.

In a special effort to study the subsurface region in the Tiran Straits between the Sinai coast and Tiran Island, Rosenberg was able to enhance considerably the data content by ingeniously developed numerical algorithms to eliminate the adjacency effects and other noise sources. Aerosols are one particular source of noise, which leads to the adjacency effect; this describes the end result caused by omnidirectional scatter of light from illuminated land surfaces into the atmosphere with some fraction rescattered upwards above darker regions, dependent upon the aerosol content.

Another characteristic source of noise is identified as system-originated: between-line patterns due to differences in different detector sensitivities. The within-line granularity noise reflects the basic single detector noise characteristics.

The particular noise-removal algorithm developed replaces each pixel value with a three-column by five-line average unless the average differs from the pixel value by more than two units, or if any of the eight adjacent neighbors differs from the central pixel point by more than three units. Rosenberg's results showed subsurface coral reefs ranging in depths from 1 to 20 m, while preserving the shoreline, which was indicated to be a region of maximum topographical gradient.

As a result of applying this algorithm, considerable success was achieved in the study of the autumn surface topography and conferred current flow patterns in the constricted region between the Sinai peninsula and Tiran Island.

Norman F. Ness
4/4/85

EUROPEAN BIOTECHNOLOGY NEWS

Professor Carl-Christian Emeis of the Technical University of Aachen, West Germany, has recently developed a bioreactor for continuous production of ethanol from low-cost raw materials and waste. The bioreactor produces 60 grams of ethanol per liter of reaction volume per hour, which is approximately equivalent to the theoretical rate of productivity. The ethanol-producing bacteria, a special type of *Zymomonas mobilis*, allow for an extremely short fermentation

time--less than 1 hour. Any raw material containing glucose, fructose or saccharose may be used for ethanol production. Additional substrates such as lactose, cellobiose, or dextrine can be used for ethanol production by adding immobilized enzymes.

* * *

Plant Genetics Systems of Belgium claims to have implanted genes providing pest resistance to crop plants which are able to produce their own insecticides. Some organisms, like the bacterium *Bacillus thruingiensis*, are known to produce proteins with pesticidal activity. The genetic material responsible for the production of toxic chemicals can be isolated and inserted into a cell of a crop plant by genetic engineering techniques. The project is cofinanced by the US chemical manufacturer Rohm and Haas.

* * *

Boehringer Mannheim Company, West Germany, plans a pilot plant for industrial production of monoclonal antibodies for therapeutic use. The 5-year research project using hybridoma techniques will receive a DM5.8 million governmental support from the Federal Ministry of Research and Technology. Boehringer cooperates in this project with the Universities of Munich and Heidelberg. Boehringer will use a patented process to obtain hybrid cells which produce antibodies in permanent cultures. For production, Boehringer will use a capillary modular bioreactor with hollow fibers.

Claire E. Zomsely-Neurath
4/15/85

LONDON POLYTECHNICS TO ESTABLISH BIOTECHNOLOGY CENTER

Three London polytechnics are pooling their resources to establish a biotechnology center, according to *Chemistry and Industry* (4 March 1985). The London Centre for Biotechnology (LBC)--a collaborative venture of the polytechnics of the South Bank, Central London, and Thames--is to receive special funding from the government-funded National Advisory Board (NAB). This amounts to £115,000 in recurrent grants plus £250,000 for capital expenditure. In addition, the inner London Education Authority is to inject a further £100,000.

Dr. Terence Burlin, director of the Polytechnic of Central London, said that a major priority of the center would be to promote "biotechnology awareness" in London's schools and colleges, as well as to develop close links with biotechnological industries. "Although we plan to explore a relationship with industry, we and NAB want the center to be firmly based within the education system before developing links."

According to *Chemistry and Industry*, the establishment of the center is only part of a series of UK joint initiatives in biotechnology. The Polytechnic of Central London is already involved in another collaborative scheme, the Institute for Biotechnological Studies (IBS), along with University College London and the University of Kent. The plan is to establish links between LCB and IBS. Also, the Leicester Biocentre has announced recently an amalgamation with the Cranfield Biotechnology Centre.

Larry E. Shaffer
4/18/85

UK ALVEY PROGRAM APPROVES IKBS PROJECTS

The UK's Alvey Directorate announced in April the approval of over 50 research projects on intelligent knowledge-based computer systems (IKBS).

IKBS research is a step in the development of a "thinking computer." By modeling human reasoning, IKBS offer the prospect of handling by computer logical inferences, estimates based on rules of thumb, and best guesses. The IKBS projects will cost about £20 million ($26 million); £12.5 million will come from the Alvey Directorate and the rest from industry. (For background on the 5-year Alvey program of research in computer science, see ONR, London, report R-11-84, and *ESN* 39-5:192-193 [1985].)

The research will focus on areas such as novel computer architectures, logic programming languages, expert systems, natural language understanding, and image interpretation. The goal is to establish the technology needed for commercial application of IKBS.

The new projects will involve 28 firms, ranging from major systems companies to small software houses, and 26 universities, polytechnics, and other research institutions.

Larry E. Shaffer
4/25/85

X-RAY TRANSFERRED THERMOLUMINESCENCE: A SURPRISING NEW PHENOMENON

Thermoluminescence (TL) is a well-known phenomenon. It is observed as a reasonably sharp-peaked radiation that is emitted as a "glow" by crystals that have embedded defect sites (charge carrier traps). The luminescence appears when the crystal is heated up.

One hardly expects surprises in such a prosaic field; yet Professor A. Halperin (Racah Institute of Physics, The Hebrew University of Jerusalem), a well-known scientist with decades of work in the area of solid state physics of crystals, has just discovered an unexpected and striking new phenomenon (seen, in some way, earlier by other researchers with amazement, but without having ever been studied and explained). He calls it x-ray transferred thermoluminescence (XTTL), and he discovered this effect during his extended research concerning the optical properties of quartz crystals. Apart from the theoretical merits associated with working on such well-known, easily modified/manipulated materials such as quartz, this type of work has definite practical applications, especially in the area of communications, since quartz crystal resonators are at the heart of electronic gear used in the megahertz frequency area--which, for example, plays a big role in satellite communication.

Halperin and his associate, Dr. S. Katz, took specifically cut plates ($2\times8\times11$ mm^3 dimension) from an electronic-grade synthetic quartz crystal. They irradiated the plates, as is customary for the creation of defect sites, for 5 minutes, at 10°K temperature with the "white" radiation of a tungsten-target x-ray source (55 kV, 18 mA operation). Upon carefully heating the crystal plates to 350°K, Halperin and Katz observed the regular TL glow, with a well-pronounced leading peak produced at 82°K. Next, they again x-irradiated the crystal for 5 minutes at 10°K, but then they warmed it up to 220°K, cooled it back to 10°K, and irradiated again for 2 minutes. The glow-curve they obtained upon slow heating up followed closely the previous luminescence-intensity versus temperature curve, with a slight enhancement of the peak at 82°K. But surprisingly, they found a new peak, at 220°K, with an intensity 100 times higher than that of the old (82°K) peak. The emission spectrum of this new and unusually strong peak fits well a Gaussian shape, peaking around 390 nm and having a half-width of 94 nm. The emission conforms with what is usually obtained in this region for regular glow peaks. A series of further clarifying experiments were done.

Halperin then realized that the observed phenomenon is caused by the x-ray-induced transfer of carriers from regular traps (filled up by ordinary x-irradiation) into extraordinary trapping levels. Indeed, the preconditions for the appearance of the 190°K peak are:

1. Prepopulation of the traps that give the regular TL in the 200°K to 300°K range.
2. Emptying of shallow traps, achieved by warming up the crystal to about 220°K, before the second low-temperature x-irradiation.

These two processes lead to the redistribution of trapped carriers, which causes the XTTL to occur.

Despite the fact that the carriers in the 190°K trap constitute only a fraction of those which populated the traps in the 200°K to 300°K range, the 190°K intensity is two orders of magnitude higher than the other TL peaks. This implies that the probability for radiative recombination of the carriers released from the 190°K traps is much higher than that from the regular traps.

An estimate gave 10^{16} photons per cm^3 in the treated sample at the 190°K glow peak. It seems likely that the emission is related to Al defect centers, whose concentration in the crystals used by the scientists is known to be about $10^{17}/cm^3$. Since the XTTL could have affected probably less than 10 percent of the Al defect centers, it can be concluded that the radiative quantum efficiency in the 190°K emission is remarkably close to one. This very high yield of radiative emission from the relevant traps can be explained by assuming that the redistribution of carriers causes some of them to get trapped at very close proximity to hole centers. Recombination may then take place via a tunneling process.

Halperin thinks that the phenomenon needs, and allows for, more extended and generalized investigations. It is also possible that the new XTTL process may have unforeseen technological applications. Halperin would like to renew his old contacts with US Navy scientists and establish channels of cooperation both in this and in other projects, including color center physics.

Paul Roman
4/4/85

MOLECULAR ELECTRONICS ADVISORY GROUP ESTABLISHED IN UK

Molecular electronics is the term used to describe a rather novel and rapidly growing area of highly multidisciplinary research that aims to use molecular materials and molecular manipulation techniques to produce improved or even entirely novel electronic devices. Application of molecular materials in devices will lead to several advantageous new features: the molecular materials used to construct a device can be modified chemically in systematic ways; they can be processed at moderate temperatures; they can yield structures of unbelievably intricate nature and with very finely controlled dimensions; and, last but not least, they can offer chemical and biological specificity. Research in this area currently has three main aspects: design and preparation of new molecular materials, study and optimization of useful properties, and development of practical devices.

Some interesting examples of new materials produced (or envisaged for production) by molecular techniques are:

- Polymeric photoconductors and semiconductors, which could be used for photocopying systems and metal-free storage battery materials.
- Organic metals and even organic superconductors, which may be of great value to connect active materials and semiconductor substrates.
- Materials that react in light or electron beams and thus permit microlithography in near-molecular dimensions.
- Completely new nonlinear electro-optic materials that combine high response and stability, so much needed in pioneering integrated optics.
- Biological molecules immobilized on a semiconductor substrate; such a device will function as a specific-target-responsive sensor.
- New liquid crystals for use in switching and memory elements.
- Photochromic, electrochromic, piezoelectric, and pyroelectric materials with unusual properties and easy production, which could be used to form high-density information storage systems, detectors, or transducers.

Since molecular electronics encompasses such a wide area, progress requires close collaboration between physicists, chemists, electronics engineers, and biologists. An effective mechanism for technology transfer from academia to the industrial environment is also crucial for success. For these reasons, the UK's Science and Engineering Research Council (SERC) established in 1980 a broad-based Molecular Electronics Discussion Group. The final report of this group recommended the establishment of a smaller, permanent advisory group to identify areas of molecular electronics where the SERC should undertake special initiatives. In response to this recommendation, a few months ago the SERC's Science and Engineering Boards jointly appointed a Molecular Electronics Advisory Group (MEAG). The mandate of MEAG is to advise the boards on a strategy for the stimulation and support of molecular electronics research. The chairman of the group is Professor Gareth Roberts, FRS, Oxford University (formerly at Durham University). Other universities involved directly are Cambridge University, the University of Manchester Institute of Science and Technology, and the University College of North Wales. Industrial representatives on MEAG come from Imperial Chemical Industries, Plessey Research, British Telecom, Pilkington Bros., and Unilever Research. The secretary of MEAG is Mr. D.M. Schildt, SERC Central Office, Polaris House, Swindon SN2 1ET, UK.

Paul Roman
3/27/85

ROYAL SOCIETY NAMES NEW FELLOWS

Dr. J.D. Murray of Oxford University and Dr. Michael Gaster of the newly organized firm British Maritime Technology have been selected as Fellows of the Royal Society. The announcement was made at the 27th British Theoretical Mechanics Colloquium in March at the University of Leeds.

Murray was one of the principal lecturers of the colloquium. He delivered a fascinating lecture entitled "The New Approach to the Generation of Biological Pattern and Form." This was a survey of work--largely performed in his laboratory--on the application of mathematical techniques to the determination of biological patterns. Gaster is very well known for his work on boundary-layer stability and transition. A report on some of his most recent work was published in *ESN* 39-1:23-25 (1985).

Patrick Leehey
4/12/85

UK TO HOST MEETING ON FINE CHEMICALS FOR THE ELECTRONICS INDUSTRY

A major 3-day international conference, Fine Chemicals for the Electronics Industry, is being organized jointly with the Fine Chemicals and Medicinals Group, Industrial Division, and the Applied Solid State Chemistry Group of the Royal Society of Chemistry. The conference will be held at the University of Bath, UK, from 2 through 4 April 1986. Speakers from overseas who have already agreed to participate include: Professor M.S. Wrighton (Massachusetts Institute of Technology), "The Chemistry of Solar Energy Conversion"; Dr. F.L. Carter (Naval Research Laboratory, Washington, DC), "The Molecular Computer"; Mr. S. Ishikawz (Canon, Inc.), "Organic Photoconductors"; Dr. J.M. Williams (Argonne National Laboratory), "Organic Superconductors."

The first circular was to be distributed in June. For further information, contact David L. Venezky at ONR, London.

David L. Venezky
4/19/85

CONFERENCE ON TRANSPARENT MATERIALS FOR OPTOELECTRONICS SET FOR DECEMBER

The main event of 1985 being organized by the Applied Solid State Chemistry Group of the UK's Royal Society of Chemistry will be a 1-day meeting, Transparent Materials for Opto-Electronics; it will be held at the Scientific Societies' Lecture Theatre, London, on 11 December. The Society of Glass Technology, the British Association for Crystal Growth, and the Optical Group of the Institute of Physics are supporting the meeting. Contributions are invited in the fields of infrared glasses and fibers, polymers for optics and fiber optics, and crystalline nonlinear optical materials.

The program organizer is Dr. R.T. Murray, ICI Electronics Group, The Heath, Runcorn, Cheshire WA7 7QE, UK.

For further information contact David L. Venezky at ONR, London.

David L. Venezky
4/19/85

THIRD EUROPEAN CONFERENCE ON PERSONALITY

The third biennial conference of the European Association of Personality Psychology will be held in Gdansk, Poland, from 10 through 13 September, 1986. The conference will concentrate on six main topics: temperament and personality; advances in personality measurement; personality changes; personality and the regulation of social behavior; theory of action and personality; and the self as a personality variable. Conference registration should be completed before 31 December 1985. All correspondence should be addressed to the Conference Secretary, Mrs. Katarzyna Korpolewska, University of Warsaw, Department of Psychology, Stawki 5/7, 00-183 Warsaw, Poland; Telex: 815439 UW PL.

Richard E. Snow
4/30/85

CNRS AIMS TO UNIFY FRENCH SCIENCE

France's Centre National de la Recherche Scientifique (CNRS) is to devote 40 percent of its resources to newly defined strategic objectives, according to a CNRS 5- to 7-year plan published in April. An article in *Nature* (2 May 1985) reports that the disciplines include many fundamental subjects (Table 1), such as nuclear and particle

Table 1

Areas of CNRS Research
(From *Nature*, Vol 315
[2 May 1985], 5)

- The universe, atomic nucleus and elementary particles (some of the costs of these disciplines are borne outside CNRS)
- Mathematics
- Optics
- Materials sciences
- *Filière électronique* (science applied to the microelectronics industry)
- Plasma physics and nuclear fusion
- Energy and thermodynamics
- Process engineering
- New methods in Earth sciences
- Dynamics of the ocean systems
- Remote sensing
- Continental water
- Understanding chemical reactions
- Chemistry-biology interaction
- Biotechnology
- Neurosciences
- Sciences of evolution
- Sciences of communication
- Employment, work, and technology
- Urbanism, architecture, and society
- Large scientific equipment

physics, but these are sometimes combined in significant new associations. Thus, the "sciences of the universe" combine in one objective with particle and nuclear physics. Other objectives specify boundary-breaking explicitly, such as that named "the interaction between and chemistry biology." CNRS director Pierre Papon has long wanted to unify the highly divided disciplines in France, according to *Nature*.

The new objectives also stress long-range applied science, such as Earth observation from satellites (in anticipation of the launch of the French SPOT satellite this year), process engineering, biotechnology and so on, but Papon said that their selection is not a threat to the basic sciences. Many of them, he said, are in fact basic science, and "it is not a major problem to defend basic science in France."

The *Nature* article notes that according to Papon, the real objective of the CNRS list is "to unify science." He said he was struck, during a European tour last year, by the many links between chemistry and biology departments in Britain, whereas there is just one such department in France. Unification of disciplines is also more advanced in Sweden and Switzerland. Research in France is more fractured than elsewhere, though many modern scientific problems are multidisciplinary.

For background on the organization of CNRS, see the article on page 341.

Larry E. Shaffer
5/7/85

ONRL COSPONSORED CONFERENCES

ONR, London, can nominate two registration-free participants in the conferences it supports. Readers who are interested in attending a conference should write to the Scientific Director, ONRL, Box 39, FPO New York 09510.

Inaugural Meeting of the European Society for Cognitive Psychology, Nijmegen, The Netherlands, 9-12 September 1985.

Technological Application of Bilayers, Vesicles, and Langmuir-Blodgett Films, Denerja, Spain, 25-29 November 1985.

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EUROPEAN VISITORS TO THE US SPONSORED BY ONRL

Visitor	Areas of Interest	Organizations to be Visited	Want Information? Contact at ONRL
Professor Kenneth Easterling University of Luleå S-951 87 Luleå Sweden	Metallurgy/Ceramics	ONRHQ (18 July 1985) DTNSRDC (19 July 1985)	Kenneth Challenger
Prof. Dr.-Ing. K. Detert Institut für Werkstofftechnik Universität Gesamthochschule Siegen Postfach 101240 5900 Siegen West Germany	Fatigue and Fracture	ONRHQ NRL Univ. of Maryland DTNSRDC Natl. Bur. of Std. (Aug 85)	Kenneth Challenger
Dr. Ian Marshall Paisley College of Technology Paisley PA1 2BE Scotland	Composite Materials	NAVWPNCEN Aeromechanics Lab. Moffet Field California (2-5 Aug 85)	Kenneth Challenger
Professor Andrea Prosperetti Physics Department Universita degli Studi 20133 Milano Italy	Physical Acoustics	DTNSRDC Courant Institute New York Univ. (6-9 Aug 85)	Charles J. Holland

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CDT Arnold Böhrer Rekruterings on Selectiecentrum Sectie Psychologisch Onderzoek Kazerne Klein Kasteeltje 9de Linielaan 1000 Brussels Belgium	Military Personnel Psychology	NAVPERSRANDCEN Univ. of Minn. ONRHQ (Aug.-Oct. 85)	Richard E. Snow
Dr. Peter Nenniger Seminar für Philosophie und Erziehungswissenschaft Albert Ludwigs Universität D-7800 Freiburg 1 BR West Germany	Cognitive Psychology of Text Analysis	NPRDC, San Diego (Aug or Sep 85) Univ. of Illinois (Sep 85) Carnegie-Mellon Univ. (Sep 85) IBM System Research Center (Sep 85) ONRHQ (Oct 85)	Richard E. Snow
Paolo Mele Università degli Studi di Roma "La Sapienza" Facolta di Ingegneria Dipartimento di Idraulica Trasporti e Strade (n 37) Via Eudossiana, 18-00184 Rome Italy	Fluid Dynamics	DTNSRDC (Sep 85) NRL (Sep 85) ONRHQ (Sep 85) MIT (Sep 85)	Patrick Leehey

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SCIENCE NEWSBRIEFS FOR APRIL AND MAY

The following issues of *Science Newsbrief* were published by the ONR, London, Scientific Liaison Division during April and May. *Science Newsbrief* provides concise accounts of scientific developments or science policy in Europe and the Middle East. Please request copies, by number, from ONR, London.

Science Newsbrief Number	Title
3-16	Israeli Meteorological Service Focuses on R&D, by LCDR Richard G. Kelley, USN.
3-17	Typhoon Predicted by Computer Model at ECMWF, by LCDR Richard G. Kelley, USN.
3-18	Spanish Researchers Take Important Step in Recycling Carbon Dioxide, by David L. Venezky.
3-20	Conference on Laminar and Turbulent Flow to be Held in Wales, by Patrick Leehey.
3-21	UK Mergers Produce New Firm, British Maritime Technology, by Patrick Leehey.
3-22	UK to Host International Conference on Mathematics in Signal Processing, by Paul Roman.
3-23	Spectral Signatures of Objects in Remote Sensing--Third International Colloquium, by LCDR Richard G. Kelley, USN.
3-24	UK Oceanographic Institute Hosts Summer Seminars, by LCDR Richard G. Kelley, USN.

APRIL MAS BULLETINS

The following *Military Applications Summary (MAS) Bulletins* were published by the ONR, London, Military Applications Division during April. The *MAS Bulletin* is an account of naval developments in European research, development, test, and evaluation. Its distribution is limited to offices with the US Department of Defense. DoD organizations should request copies of the *Bulletins*, by number, from ONR, London.

MASB Number	Title
35-85	ECMWF Products for International Use
36-85	European Space Update
37-85	New Material for Shielding Against Electromagnetic Fields
38-85	ERS-1 Announcement of Opportunity
39-85	MATRA Family of Air-Air Missiles--Magic to MICA
40-85	Greenland-Iceland-Norway Sea Study--A NATO Proposal
41-85	European Aerospace Update
42-85	Magazine Torpedo Launch System

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ONRL REPORTS

To request reports, check the boxes on the self-addressed mailer and return it to ONR, London.

R-1-85 *Space Research in the United Kingdom: An Assessment*, by Norman F. Ness. This report examines the history and funding of UK space research; discusses work in disciplines such as astronomy and astrophysics, solar system studies, and terrestrial studies; and considers prospects for the future.

C-3-85 *Electromagnetic Compatibility Conference Features Biological Interactions*, by Thomas C. Rozzell. The Sixth Symposium and Technical Exhibition on Electromagnetic Compatibility was held in Zurich, Switzerland, in March 1985. This report deals with a session on the interaction between electromagnetic (EM) waves and biological systems. The papers were on topics such as the hazards of EM fields, stationary magnetic fields, therapeutic techniques, microwave power dissipation, and measurement of specific absorption rate.

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